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## IN THIS ISSUE

- Editorial—Licensure of BCG Vaccine  
Further Observations on Histoplasmosis



FEDERAL SECURITY AGENCY

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PUBLIC HEALTH SERVICE

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**CONTENTS**

	Page
Editorial—Licensure of BCG vaccine. Robt. J. Anderson	963
Further observations on histoplasmosis. Mycology and bacteriology. Michael L. Furelow	965
<b>INCIDENCE OF DISEASE</b>	
United States:	
Summary of reports from States	995
Deaths during week ended July 15, 1950	996
Table of reported cases of communicable diseases	997
Foreign reports:	
Anglo-Egyptian Sudan—Meningitis, meningococcal	999
Egypt—Meningitis, meningococcal	999
Cuba—4 weeks ended May 27, 1950	999
Finland—May 1950	999
Madagascar—May 1950	1000
Cholera	1000
Plague	1000
Smallpox	1000
Typhus fever	1001
Yellow fever	1001
Plague infection in fleas on the Island of Hawaii.	1001
Study of laboratory infection	1002

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## —Editorial—

### Licensure of BCG Vaccine

On July 12, the Public Health Service licensed the Research Foundation and the University of Illinois for "manufacture, exportation, importation and sale" of BCG. Until now, licensure of the product has awaited manufacture in accordance with certain requirements. In view of the divergence of opinion about this biological product, it seems in order to consider the significance of such action. It means that the vaccine produced by the licensed laboratory has been found safe by trial with animals, that it is free from contaminating substances, and that it will produce a satisfactory immediate reaction in animals and human beings when used within the prescribed time limit. Thus, the vaccine may enter interstate commerce and will be available to health officers and clinicians who wish to use it as a protective measure against tuberculosis.

In those places of the world where tuberculosis is a national emergency and where prosecution of the usual control methods is impossible, it is understandable that BCG has been given extensive application. In this country, where we are not faced with the same deficiencies, the medical profession for the most part has not advocated the widespread usage of the vaccine. The Council on the Management and Treatment of Diseases of the Chest, reporting for the American College of Chest Physicians, has recommended that the use of BCG vaccine be restricted to controlled studies (1). The American Trudeau Society (2) recommends that the use of BCG be limited to groups especially exposed to the risk of tuberculous infection.

The Public Health Service, like others concerned about tuberculosis, would welcome any agent which would prevent the personal tragedy and public health problem of tuberculosis. But it has not yet been conclusively demonstrated that BCG is such an agent.

This is the fifty-fourth of a series of special issues of PUBLIC HEALTH REPORTS devoted exclusively to tuberculosis control, which appear in the first week of each month. The series began with the Mar. 1, 1946, issue. The articles in these special issues are reprinted as extracts from the PUBLIC HEALTH REPORTS. Effective with the July 5, 1946, issue, these extracts may be purchased from the Superintendent of Documents, Government Printing Office, Washington 25, D. C., for 10 cents a single copy. Subscriptions are obtainable at \$1.00 per year; \$1.25 foreign.

Moreover, efforts to find more stable and suitable immunizing agents are going forward. Indiscriminate use of BCG here could, we believe, not only negate its potential future application but might divert attention from the control activities which are serving the Nation well and which, under the circumstances prevailing in the United States, could lead to the virtual eradication of tuberculosis. It is our feeling that we must be very careful not to imperil the gains we are making with proved control methods, and must not relax in any area the pursuit of case finding and treatment to care for the sick and to protect the well.

If the use of BCG in the United States is to contribute more information than has been gained in almost 30 years of use elsewhere, vaccination programs must be carefully planned. It would be desirable if State and local health departments which are immediately responsible for tuberculosis control were to develop plans for the use of the vaccine in their jurisdictions and keep records of those who are vaccinated. A beginning has been made in Wisconsin where the State Health Department has reviewed all requests for the vaccine desired from research laboratories, and in New York where the State Department of Health has manufactured BCG vaccine and has kept records of persons in the State who were vaccinated.

We feel that mass BCG vaccination campaigns are not indicated in this country where tuberculosis morbidity and mortality rates are relatively low (3). It is our recommendation that vaccination be limited to those persons who are particularly vulnerable to exposure. These include:

1. Those physicians, nurses, laboratory workers, hospital employees, and others who are exposed by occupation.
2. Those individuals or groups exposed to continued contact with tuberculosis.
3. Patients, inmates and employees of institutions, such as mental hospitals and prisons, in which case-finding programs indicate that exposure to tuberculosis is likely to be high.

ROBT. J. ANDERSON, *Medical Director,  
Chief, Division of Tuberculosis.*

#### REFERENCES

- (1) Joint meeting of Council on the Management and Treatment of Diseases of the Chest and Council on Public Health of American College of Chest Physicians, San Francisco, June 22, 1950.
- (2) ATS Statement on BCG. *Am. Rev. Tuberc.*, **60**: 681-682 (1949).
- (3) Anderson, Robt. J. and Palmer, Carroll E.: *BCG. J. A. M. A.*, **143**: 1048-1051 (July 22) 1950.

## **Further Observations on Histoplasmosis**

### **Mycology and Bacteriology**

By MICHAEL L. FURCOLOW, M. D.\*

Recent studies of the fungus *Histoplasma capsulatum* have indicated that human infection with the organism may manifest itself in a variety of ways. The largest number of people affected, however, fail to show any clinical symptoms of the disease, and the only evidence that an infection has been present at some time in the past is sensitivity to the skin-testing antigen, histoplasmin, and quite frequently, calcified areas in the lungs or hilar lymph nodes. Findings of this nature are most common in the States bordering the Mississippi River and its larger tributaries, particularly in the Kansas City area where about 80 percent of the population are positive histoplasmin reactors (1, 2, 3).

With an infection so common in a subclinical form, one would expect to find at least a few instances of clinical disease. And, indeed, cases of fatal histoplasmosis have been reported from time to time. More recently, too, histoplasmosis has been diagnosed in patients who recovered from severe clinical infections with the fungus (4-12).

An earlier publication by Bunnell and Furcolow (4) reported on ten patients in the Kansas City area from whom *H. capsulatum* was recovered. The clinical material was presented with respect to the outcome of the disease in order to indicate that the infection is not invariably fatal, as was formerly thought.

During the last 2 years, an attempt has been made to obtain further information about clinical infection with *H. capsulatum* in the Kansas City area. From the large number of hospital and private patients referred as histoplasmosis suspects, those who showed a positive serological reaction to the histoplasmosis complement fixation test were selected as subjects for study. These patients were examined repeatedly by various tests in a search for the etiologic organism. However, it was not always possible or appropriate to follow the same procedure with all patients, since the type of examination very frequently depended upon the pathological condition from which the patient suffered. In some instances, sputum, gastric aspirations, or tissue biopsies were available for study, while in others, bone marrow aspirations were obtained for culture and animal inoculation. When

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autopsy material was available, tissue sections and pooled organs were studied pathologically, bacteriologically, and by animal inoculation.

The six patients selected for discussion in this paper are those from whom at least one specimen was found to be positive for *H. capsulatum*. The complete clinical histories of these patients, when added to the previously published cases, indicate that, in the Kansas City area, the fungus *H. capsulatum* may be found in some patients who are clinically sick either with histoplasmosis or some other, possibly unrelated disease. Such findings indicate that the fungus may be found in a wide variety of clinical conditions without reference to a diagnosis of histoplasmosis.

In the light of this observation, it would be interesting to know how often the organism could be found in apparently healthy people if the search for the fungus were as diligent as it was in the subjects of this study. One might speculate, too, on the possible relationship of histoplasmosis to other granulomatous diseases, Hodgkins disease for example, where the etiology is still unknown. Certainly, one of the most pressing questions is how to evaluate the diagnostic significance of the recovery of the fungus in the presence of another disease. Should it be considered an incidental finding of academic rather than practical importance, or does the presence of the fungus influence in some way the onset or course of the predominant clinical disease?

In the clinical histories which follow, information about the six new patients (cases 11-16) is presented in terms of the certainty and possible significance of the diagnosis, rather than in terms of survival, as in the earlier case report study. Follow-up reports of the five surviving patients in the previous group (cases 1-5) are also included to bring the information up to date.

### Previously Reported Cases

**CASE 1.** C. D., white male, age 13 when first seen in February 1945. When discovered in a survey of school children in Kansas City, he was found to have miliary pulmonary infiltrations with bilateral hilar adenopathy (fig. 1), and positive histoplasmin and negative tuberculin skin tests. In spite of X-ray findings, he was essentially in good health. After 10 days' hospitalization, he was discharged and kept under supervision for laboratory examinations. *H. capsulatum* was grown from a culture of a gastric specimen in November 1945. Follow-up skin tests on October 4, 1948, showed a negative reaction to tuberculin and blastomycin, but a positive reaction to histoplasmin. The blood complement fixation tests have been suspicious (+++) or (++) on five occasions, and negative once since the last report. No further efforts have been made to isolate any organisms, as the film (fig. 2) shows miliary calcifications, almost completely healed, with very little infiltration surrounding the calcified lesions. This boy is still in good health and was attending school in March 1950.

**CASE 2.** W. B., white male age 5 months when admitted to the hospital in March 1947 with fever, otitis media, hepatomegaly and splenomegaly. Cultures

of blood and sternal marrow obtained on the 20th hospital day were positive for *H. capsulatum*. Slow improvement followed 7 weeks of spiking fever, and the patient was discharged after 9½ months of hospital care. This child has continued to be in excellent health (except for one cold) and has gained 11 pounds since discharge from the hospital December 30, 1947. His chest film has never showed any abnormal shadows; a follow-up film on January 16, 1950, was still negative. He has had one negative tuberculin and three positive histoplasmin skin tests since the last report. Of six complement fixation tests, three were positive, two suspicious, and the most recent one (January 1950) negative.

CASE 3. S. P., white female, age 20 months when seen March 23, 1947. Four months before hospitalization, she had a febrile episode described as influenza, followed by malaise and abdominal distension. On admission, she had fever, anemia, and enlargement of the liver, spleen, and peripheral lymph nodes. The chest film revealed an infiltration in the right base, and right hilar adenopathy. On the 90th hospital day the spleen was removed, and positive cultures for *H. capsulatum* were obtained from the surgical specimen as well as from later gastric aspirations. This child has exhibited continued improvement since the operation. She has been well, gaining weight, and is free of symptoms. Skin tests August 16, 1949, showed negative tuberculin and positive histoplasmin reactions, while a chest film February 18, 1950, revealed definite calcification in the right base and hilar lymph nodes. (These X-rays are not presented because of their unsatisfactory reproduction quality). Complement fixation tests October 18, 1948, August 16, 1949, and February 18, 1950, were negative.

*Comment.* As noted, the disease was mild in case 1 and severe in cases 2 and 3. Complement fixation tests and histoplasmin skin sensitivity tests were positive, and diagnosis was confirmed in all three cases by recovery of the fungus during the illness.

CASE 4. G. M., white male, age 52. This patient was referred for study in October 1947, because of unexplained pulmonary lesions (fig. 3), negative tuberculin and positive histoplasmin skin tests and a positive (++++) complement fixation for histoplasmosis. The patient continues to be chronically ill with recurrent attacks of what he calls "influenza." These are characterized by fever (102°–103°), cough, anorexia, and increased sputum production. His weight has fallen progressively from 129 pounds in January 1948 to 104 in April 1950. He continues to have an elevated afternoon temperature, but is able to get about the house and to take occasional rides in his car. Further laboratory work since the last report includes 5 guinea pig inoculations which were negative for tuberculosis and negative cultures for tubercle bacilli on 10 sputum specimens, 2 gastric washings, and 1 skin biopsy; 11 out of 16 sputum specimens were positive for *H. capsulatum*, while 2 gastric washings and 1 bronchoscopy specimen were negative for fungi; 4 of 9 mice and 1 of 7 rats inoculated with the sputum specimens were positive for *H. capsulatum*. Blood complement fixation tests were positive on 10 occasions, the last of which occurred October 6, 1949. The chest film shows slowly progressive increase in the bilateral disease with cavitation in both lungs (fig. 4).

*Comment.* This case is of particular interest because of the similarity to chronic, slowly progressive, cavitary tuberculosis. However, repeated laboratory examinations have failed to demonstrate tubercle bacilli. Histoplasmin sensitivity, the presence of complement-fixing

antibodies, and positive sputum cultures for *H. capsulatum* corroborate the diagnosis of histoplasmosis.

CASE 5. R. J., white male, age 64. Additional history obtained since the previous report reveals that this man was admitted to a hospital June 3, 1943, because of cough, dyspnea, and loss of weight. An X-ray at that time showed bilateral apical infiltrations with possible cavity in the right first interspace, pleuritic changes in the right base and mediastinal shift to the right (fig. 5). He was referred to a tuberculosis sanatorium with a diagnosis of far-advanced tuberculosis (without laboratory work), but he refused to go. His next brief stay in the hospital (December 5, 1947, to January 7, 1948) was described earlier. On November 25, 1948, he became comatose while eating dinner and was readmitted to the hospital for several weeks. No new physical findings were noted at this time. Although his general condition was poor, he left against advice, but was persuaded to return on April 18, 1949, for a course of bacillomycin (Wyeth). At that time, there was extensive cavitation in the right lung, with marked retraction of the mediastinum to the right, scattered fibrocalcific lesions in the left with emphysema and residual apical pleural changes (fig. 6).

Skin tests again showed a positive reaction to histoplasmin and a negative reaction to tuberculin. Blood studies revealed a sedimentation rate of 33 mm.; red cell count of 3,900,000 per cu. mm., with 10.5 grams of hemoglobin; white cell count of 15,000, with 83 percent polymorphonuclear leukocytes; and a positive (++++) complement fixation test. Bacillomycin, 100 mg., with 2 percent procaine, was given intramuscularly every 6 hours beginning April 19, 1949, but was discontinued after 48 hours because of intense cellulitis at the site of injection and general malaise, chills, and fever. Thereafter, the patient seemed to improve on sulfadiazine therapy, but on May 1, 1949, he suddenly developed convulsive seizures and died. During his various admissions, a total of 24 sputum specimens were negative on culture for tubercle bacilli, while 13 out of 17 sputum cultures were positive for *H. capsulatum*. Two gastric specimens were negative for tubercle bacilli, and 1 out of 5 were positive for *H. capsulatum*. Animal inoculations with sputum specimens were positive for *H. capsulatum* in 4 of 14 mice and 6 of 6 rats, while 8 guinea pigs were negative for tuberculosis.

Autopsy revealed histoplasmosis of lungs, adrenals, and spleen, and no evidence of tuberculosis.

*Comment.* This is another cavitary case in which autopsy examination confirmed the diagnosis of histoplasmosis.

The only new finding that can be reported now on case 6 is that organisms typical of *H. capsulatum* have been identified pathologically in lung tissue. Tuberculosis was also diagnosed in this case, in which the lesion was confined to the right lower lobe (fig. 7).

No follow-up material is given for cases 7-10 since these patients died prior to publication of the previous paper and their reports were complete. However, X-ray reproductions are presented for cases 7, 8, and 10 (figs. 8-11).

For case 7 (figs. 8 and 9) both tuberculosis and histoplasmosis were proved at autopsy. Case 8 (fig. 10) was diagnosed at autopsy as Hodgkins' disease and histoplasmosis. Case 10 (fig. 11) represents a case of disseminated histoplasmosis proved by autopsy.

## New Cases

### Severe Clinical Illness With Recovery

CASE 11. D. S., white male, age 4 years. This child has lived all his life on a farm bordering the Kansas River, about 36 miles northwest of Kansas City. When referred for study, he was recovering from an illness diagnosed as miliary tuberculosis.

**History.** Patient had rapid breathing, cough, fever, and abdominal pain 3½ weeks before admission, and symptoms persisted in spite of sulfadiazine and penicillin treatment. He was admitted to a neighboring hospital August 22, 1946, where examination revealed dyspnea, enlarged spleen, and fever of 103°. X-rays showed multiple patches of increased density in both lungs, suggesting miliary tuberculosis. Temperature spiked up to 104° the first 2 days, then went gradually lower, with daily spikes of at least 101° during the entire 16 days of hospitalization, although the patient improved clinically. A tuberculin test proved negative, while a histoplasmin skin test was doubtful (erythema only). The parents' X-rays and tuberculin tests were negative. Patient was referred for further study.

**First admission.** September 11, 1946. Examination was essentially negative except for palpable spleen. Chest X-rays revealed miliary, soft infiltrates throughout both lungs and enlarged hilar lymph nodes (fig. 12). The patient's temperature occasionally rose to 99° during the hospital stay. The red blood cell count was 3,650,000 per cu. mm., with 12 grams hemoglobin; and the white cell count was 12,900 with 54 percent polymorphonuclear leukocytes, 38 percent lymphocytes, 2 eosinophils, 2 basophils, and 6 monocytes. The erythrocyte sedimentation rate was 35 mm. in 1 hour. Urine was negative. The patient was discharged after 6 days.

**Second admission.** October 16–19, 1946 (to obtain 3 gastric washings for culture). The patient's temperature continued to rise in the afternoon to 99°. He still complained of occasional headaches and malaise. Examination revealed that the tonsils were enlarged and infected, and that both the liver and spleen were easily palpable. X-ray showed the continued presence of miliary infiltrations which appeared to be somewhat more clearly defined and "harder."

Blood count showed 5,140,000 red blood cells per cu. mm., with 84 percent hemoglobin, and 12,500 white blood cells with 39 percent polymorphonuclear leukocytes, 57 percent lymphocytes, 1 eosinophile, and 2 monocytes.

**Skin tests.** Tuberculin skin tests were negative on August 25, 1946 (during the first illness) and on five subsequent occasions, the last of which was in August 1947. The parents had negative tuberculin tests and chest X-rays. The patient's histoplasmin test was doubtful (erythema only) on August 25, slightly positive on September 11, and definitely positive on October 17, 1946. Three subsequent positive tests were reported, the last of which occurred in August 1947. Two tests with blastomycin were negative, as were tests with extracts of *Alternaria* and *Hormodendron*.

**Complement fixation tests.** Blood obtained on August 12, 1947, showed a positive (++++) complement fixation test, as have four subsequent blood samples. The last blood test (December 28, 1949) proved suspicious (+++).

**Mycology and bacteriology.** During the two hospital admissions, smears and cultures for acid-fast organisms were performed on five gastric specimens. One hamster was inoculated with these specimens and was negative at autopsy. Ten gastric and one bone marrow specimens, two nose and throat cultures, and four blood cultures were negative for pathogenic fungi. Culture of the tonsils (removed January 29, 1948) revealed typical colonies of *H. capsulatum* on several

plates. Autopsy examination of four mice inoculated with tonsillar tissue proved negative, as did culture of organs.

*Course.* The patient improved progressively during observation. His spleen gradually regressed, afternoon fever disappeared, and he showed progressive gain in weight. By April 22, 1947, the sedimentation rate was normal, and the chest X-ray showed the lesions to be well defined and nodular. By January 1948, calcification had appeared in the center of the infiltrates. By December 1949, much of the soft infiltrate surrounding the calcified centers had disappeared and the picture was typical of "miliary calcification," with more than 100 separate small calcified areas visible in each lung field (fig. 13).

On the routine visit in January 1948, the patient's mother stated that the child's local physician had advised the removal of his tonsils because of repeated attacks of upper respiratory infection. This was done on January 28, 1948, and the tonsils were placed in saline solution and shipped to the laboratory where they were received the next day. Cultures of these tonsils were positive for *Histoplasma*. Pathological study revealed granuloma, but *Histoplasma* have not been definitely identified. The subsequent course of the patient's illness to the point of recovery was uneventful. When last seen on December 28, 1949, the patient weighed 68 pounds and appeared in excellent health.

*Comment.* One of the most interesting aspects of this case is the way in which the etiological agent was found—culture of tonsils removed 18 months after the acute onset of disease. All other attempts to isolate a causative agent failed. Nevertheless, the chest film showed evidence of an active, widespread inflammatory process, similar in appearance to that of case 1 (fig. 1), where a positive culture was found from gastric washings. The difficulty of recovering organisms from sputum or gastric washings in cases where there is apparently a great deal of scattered infection throughout the lungs cannot be explained at this time.

#### *Moderately Severe Clinical Illness With Recovery*

CASE 12. E. A.,<sup>1</sup> white female, 41 years old. This patient, a housewife, lived in Chase County, Kans., for 30 years before moving to southern California, where she lived for 11 years. In November 1948, she returned to Chase County and then settled in southern Missouri in January 1949. She was studied because of atypical findings in her X-ray.

*History.* The patient now lives in a house which, up to the time she occupied it in January 1950, had been vacant for 3 or 4 years. This was an oak clapboard house which was unpainted when the patient moved in and contained a great deal of dust, debris, some rotting wood, and many mud-wasps' nests. It was located in scrub-oak timber about 5 miles from a paved highway. From January 1 until the onset of her illness, the patient was engaged in house cleaning, sweeping, and removing wallpaper.

On March 22, one day after exposure to rain, the patient suffered from fever and chills. Her temperature rose to 102° and was accompanied by sweating, chest pain, and a nonproductive cough.

This condition persisted for about 3 days without change. When she failed to improve, the patient consulted a physician March 25, 1949. Physical examina-

<sup>1</sup> Reported through the courtesy of Mrs. Ilse Heilbrunn and Dr. A. R. Cain, Lockwood Memorial Hospital, Lockwood, Mo. They will report this case in detail later.

tion at this time showed injection of the posterior pharynx and right cervical lymphadenopathy. Urine examination was negative, and blood agglutinations were negative for tularemia, typhus, and undulant fever. A diagnosis of upper respiratory infection was made and a cough syrup was prescribed.

The patient continued to have fever (up to 102°), with chills, chest pain, and a much harder cough. She consulted her physician again 5 days after the first visit and he referred her to the hospital.

*Admission findings.* April 1, 1949. Physical findings were essentially negative. A blood count showed 4,350,000 red blood cells per cu. mm. with 12 gm. hemoglobin, and 11,150 white blood cells per cu. mm. with 48 percent polymorphonuclear leukocytes, 25 percent lymphocytes, 3 percent monocytes, and 3 percent eosinophils. Repeat counts showed no marked change. Agglutination tests for tularemia, typhus, and brucellosis were again negative April 12, 1949. Urine was negative. The first X-ray taken on admission showed multiple, ill-defined areas of infiltration in both lung fields and pleurisy at the left base (fig. 14).

*Skin tests.* Tuberculin and histoplasmin skin tests were positive on two occasions—April 16 and May 16, 1949. Coccidioidin skin tests were negative twice, as was one blastomycin skin test.

*Complement fixation tests.* Sera of April 7, April 19, and September 21, 1949, gave a positive (++++) complement fixation for histoplasmosis, while those obtained on May 17, June 29, July 15, 1949, and February 17, 1950, gave a suspicious (+++) complement fixation. Serum of May 23, 1950 was negative.

*Mycology and bacteriology.* A small specimen of sputum was obtained April 7, 1949, and was received in the Kansas City laboratory the following day. This yielded positive cultures of *H. capsulatum*. Sputum was reported as negative for tubercle bacilli by the Missouri State Public Health Laboratory.

*Course.* The patient's temperature was 102° on admission to the hospital (April 1, 1949). She received duracillin, 1 cc., intramuscularly twice a day for 6 days, and 1 gram sulfadiazine every 4 hours. Her temperature gradually fell to normal, and she was discharged after 10 days. She produced very little sputum throughout the course of her illness. X-rays taken 5 days after admission revealed that the pleurisy at the left base had disappeared and definite clearing of the lung lesions was evident by April 9, 1949. Clearing was more marked by April 15, 1949, and by July 3, 1949, the lungs were largely cleared although several small infiltrates could be outlined upon close inspection. These appeared to be definitely "harder" and more circumscribed than on the original films. By December 8, 1949, only a small fibrotic strand in the left second interspace could be seen.

On or about April 20, the patient developed pain in the left wrist following a strain. Later, pain and swelling appeared in the right wrist, elbow, and shoulder; and still later in the right ankle. Subsequently, the left ankle developed pain and swelling as well. The pain and swelling gradually disappeared from all parts except the ankles, which were still painful and swollen on June 29.

About April 27, a rash which resembled poison ivy appeared on the patient's right forearm and hand. Large blisters developed and slowly disappeared in the course of 3 weeks. These symptoms resembled in every way the patient's previous attacks of poison ivy.

About May 1, hard red "bumps" developed under the skin in the left calf. Later, a number of these developed about the left ankle, and then one appeared on the right calf and another on the inner aspect of both knees. One also developed on the shin. These lesions were red, firm, and indurated, slightly painful, and up to one-half inch in diameter. They disappeared slowly during the last week in May.

At the present time (March 1950), the patient has no complaints and feels well.

Her cough and chest pain are completely gone and she is carrying on her normal work as a housewife.

*Comment.* This case is considered probable histoplasmosis because of the clinical picture of an acute respiratory infection following exposure to dust, positive complement fixation and skin tests, recovery of the fungus in a sputum specimen taken during the height of the infection, and the rapid resolution of the pulmonary infiltrates. It will be interesting to follow this patient to see if calcification occurs during the next few years. Unfortunately, studies for tuberculosis were not complete in this case. The migratory type of arthritis which occurred 3 weeks after the first injection of duracillin was thought to be an allergic type of reaction to the antibiotic.

#### *Moderately Severe Clinical Illness, Recovery Questionable*

CASE 13. W. W.,<sup>2</sup> white male, 64 years old. This patient, a laborer, had lived for 11 years in Kansas City about 30 years ago, but had since lived in the southeastern part of Kansas, some 200 miles from Kansas City. He was studied because of a positive complement fixation test for histoplasmosis.

*History.* The patient complained of hoarseness of 9 months' duration, associated with cough and sputum, which was occasionally tinged with blood. For 6 months he had had occasional chest pain on the right side and had lost 25 pounds. There was no significant past history of pulmonary disease except for an uncomplicated pneumonia in 1944.

*Admission findings.* September 6, 1949. Patient was well-developed but had marked hoarseness, barrel chest, and clubbing of the fingers. Breathing was diaphragmatic, with considerable intercostal retraction, and there were rales in the right base. Liver and spleen were not palpated. Temperature was 98.8° on admission. The red blood count was 5,000,000 per cu. mm. with 72 percent hemoglobin; and the white blood count was 9,500 with 72 percent polymorphonuclear leukocytes, 20 percent lymphocytes, 3 eosinophils, and 5 monocytes. The sedimentation rate was 24 mm. in one hour (Cutler method). Urine and Wasserman were negative. X-rays of the chest showed infiltration in the left lower lobe, with enlarged left hilar lymph nodes (fig. 15). There were some pleural changes in both bases.

*Skin tests.* Tuberculin skin tests were negative and histoplasmin tests positive on the 69th, 92d, and 125th day of hospitalization. Blastomycin and coccidioidin skin tests were negative on the 92d day.

*Complement fixation tests.* Sera obtained on November 17, 1949 (72d hospital day), November 28, December 7, 14, and 28 all gave a positive (++++) complement fixation for histoplasmosis. Nine subsequent tests (the last on February 27, 1950) were positive (++++) on three occasions, and suspicious (++) or (+) on six.

*Mycology and bacteriology.* Seventeen sputa were negative for acid-fast organisms by smear, and 2 were negative by concentration. Four cultures for acid-fast organisms were negative, as was guinea pig inoculation. Nine of 15 sputum specimens were positive for *H. capsulatum* by culture. Fifteen mice were inoculated with sputum, of which five were positive for *H. capsulatum*. One laryngeal biopsy culture was negative for fungi.

*Course.* The admission diagnosis was carcinoma of the larynx or tuberculosis. On the 20th hospital day the diagnosis of inoperable carcinoma of the larynx

<sup>2</sup> Reported through the courtesy of Dr. Sam Roberts, Kansas City, Mo.

was made by direct laryngoscopic examination. Biopsies of that date and of the 58th day were diagnosed as probable tuberculosis because of the presence of acute and chronic granulation tissue, although no acid-fast organisms were found. Later study of the slides revealed the presence of many doubly refractile cells typical of *H. capsulatum* in the mononuclear and giant cells. A third biopsy January 4, 1950, showed similar findings. On the 25th hospital day the patient was transferred to the tuberculosis ward, where he received streptomycin (0.5 gm. twice daily) for 42 days, followed by dihydrostreptomycin (0.5 gm. once daily) for 42 days. His temperature varied between normal and 100°, and persisted at 99° most of this time. His sputum decreased in amount although it remained profuse. On the 96th hospital day January 4, 1950, the dihydrostreptomycin was discontinued and another laryngeal biopsy was performed. Following this, tracheotomy was necessary because of edema of the larynx. The patient improved, and tracheotomy tube was finally removed on the 129th hospital day. A film of January 31, 1950 showed marked clearing of the left lower lobe (fig. 16). Patient was discharged, much improved, on March 9, 1950, after 160 days in the hospital, and was to return only for out-patient observation. His hoarseness and cough had disappeared and his general appearance had improved greatly.

*Comment.* Although the admission diagnosis in this case was laryngeal carcinoma, biopsy sections were thought to show tuberculosis, and the patient was treated with streptomycin. When positive complement fixation tests for histoplasmosis were encountered, however, the laryngeal sections were re-examined and typical *H. capsulatum* organisms were seen in the phagocytic cells. Positive sputum cultures later confirmed the diagnosis of histoplasmosis.

#### **Severe Clinical Illness with Death from Embolism**

CASE 14. G. P.,<sup>3</sup> a 69-year-old farmer who had lived all his life on farms within 32 miles of Kansas City. He was studied because of a positive complement fixation test for histoplasmosis.

*History.* The patient had had asthma all his life. For the past 10 years he had had gradual onset of fatigue, weakness, cough, shortness of breath, and pain in the chest. These symptoms became progressively worse, and the patient was finally unable to work. He had also noted gradual onset of nocturia and had for several years experienced difficulty in urinating. About 8 weeks before admission, he had had an acute episode of fever and pain in the left side of the chest and had suddenly become hoarse. One month before admission, he had been admitted to another hospital where he remained 11 days. He ran a low grade fever (up to 101°) during hospitalization, and his general condition remained unchanged. X-rays of his lungs showed "generalized granularity throughout both lung fields." Electrocardiogram suggested auriculo-ventricular conduction defect. Laryngoscopy revealed a mass which was diagnosed as carcinoma of the larynx. Biopsy of this mass was reported as suspicious of malignancy. Three sputum smears for acid-fast bacilli were negative.

*Admission findings.* December 13, 1949. Temperature was 101.4°, voice was very hoarse, patient had marked hearing difficulty, and there were rales and impaired resonance at the base of the right lung. Liver and spleen were not felt. Laryngoscopic examination revealed granulomatous involvement of the right vocal cord, with edema of the larynx. The red blood cell count was 5,330,000 per cu. mm. with 78 percent hemoglobin. The white blood count was 7,400 with

Reported through the courtesy of Dr. A. W. Eklund, Pleasant Hill, Mo.

74 percent polymorphonuclear leukocytes, 18 percent lymphocytes, 1 eosinophil, 1 basophil, and 6 monocytes. Urinalysis was negative. X-rays of the chest showed the same diffuse granularity throughout both lungs which had been previously noted. (Films were not suitable for reproduction.)

*Skin tests.* Tuberculin test was negative and histoplasmin test positive 1 month before admission and on the day of admission. Blastomycin and coccidioidin tests were also negative on the day of admission.

*Complement fixation tests.* Serum drawn November 16, 1949, gave a positive (++++) complement fixation for histoplasmosis. Five subsequent sera have given the same result, including serum obtained post mortem.

*Mycology and bacteriology.* Review of the sections removed at biopsy of the larynx November 18, 1949 revealed the presence of intracellular organisms typical of *H. capsulatum*. Eight sputum specimens were negative for acid-fast bacilli by smear, as were six by culture. One guinea pig was negative for tuberculosis. Twenty of twenty-two sputa were positive for *H. capsulatum*. Four of six mice inoculated with sputum were also positive. Combined portions of both lungs and both adrenals obtained post mortem were negative for tuberculosis by culture and guinea pig inoculation. *H. capsulatum* was cultured from blood and from eight tissues (brain, combined lungs, liver, spleen, heart, larynx, mediastinal lymph node, and combined adrenals) obtained post mortem. Two mice were injected with the combined tissues and were found positive for *Histoplasma*.

*Course.* The patient's temperature, which was 101° on admission, continued to rise daily to 100° or 101° during his entire hospital stay. He had a persistent cough, with sputum. He received 50,000 units of penicillin every 3 hours. On the third hospital day, retention of urine was noted and an indwelling catheter was inserted. Electrocardiogram revealed right bundle branch block. Swelling of both feet and lower legs was noted on the fifth hospital day, but this subsided under hot wet packs and elevation of the legs. Sulfadiazine and urea were started on the ninth hospital day, and on the same day bacillomycin (50 mg. per cc.) was started by aerosol. There was no immediate reaction, but the bacillomycin was discontinued after 4 days because of respiratory distress. On December 27 (14th hospital day) the patient suddenly developed cyanosis and difficulty in breathing, followed by collapse and death.

*Autopsy findings.* Thrombosis of the right iliac vein, with pulmonary embolism, granulomatous laryngitis and tracheitis, caseation necrosis of both adrenal glands, and hypertrophy of the prostate. Microscopic examination revealed the presence of typical *Histoplasma* organisms throughout all the tissues.

*Comment.* As in the immediately preceding case, this patient was admitted with a diagnosis of laryngeal carcinoma and biopsy sections were interpreted as showing changes probably consistent with malignancy. Positive histoplasmosis complement fixation tests, however, suggested a review of the tissue slides which were seen to contain intracellular organisms morphologically identified as *H. capsulatum*. Repeatedly positive sputum cultures, as well as autopsy findings, confirmed the diagnosis of histoplasmosis.

#### *Slight Clinical Illness with Death Due to Heart Disease*

CASE 15. J. L., white male, 61 years old. The patient, a mechanic, had lived in Kansas City for 1 year. He had spent all the rest of his life in two small towns in southeast Kansas within 125 miles of Kansas City. He was studied because of X-ray findings suggestive of tuberculosis, a negative tuberculin test, and positive histoplasmin skin test.

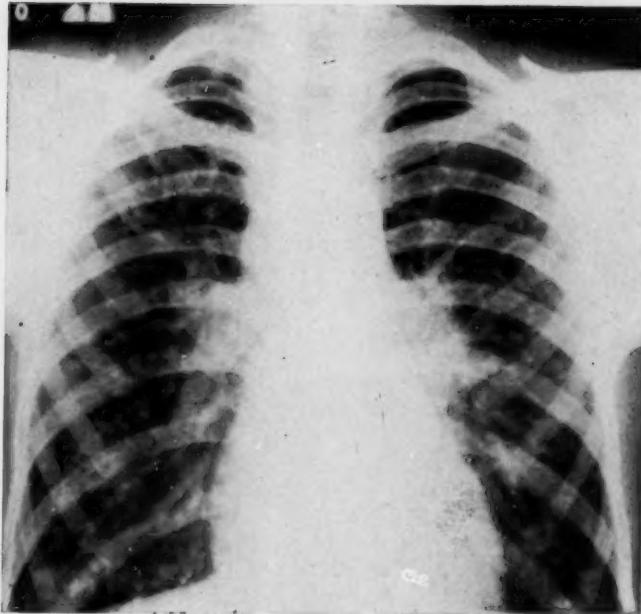


Figure 1. Case 1, April 10, 1945. Soft infiltrations throughout both lung fields with enlarged hilar nodes bilaterally.



Figure 2. Case 1, June 22, 1949, 4 years later. Calcifications throughout the lungs and in the hilar nodes.

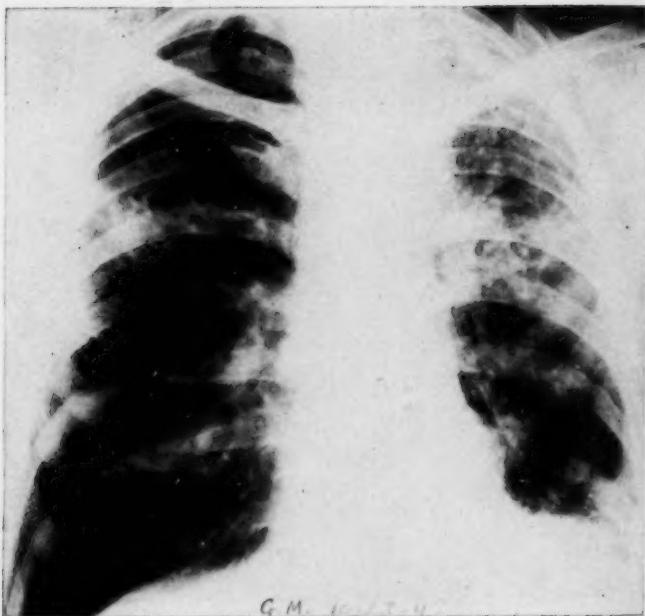


Figure 3. Case 4, October 23, 1947. Infiltrations in the left lung with questionable cavitation, pleuritic changes in the base and early spread to the right mid-lung field.

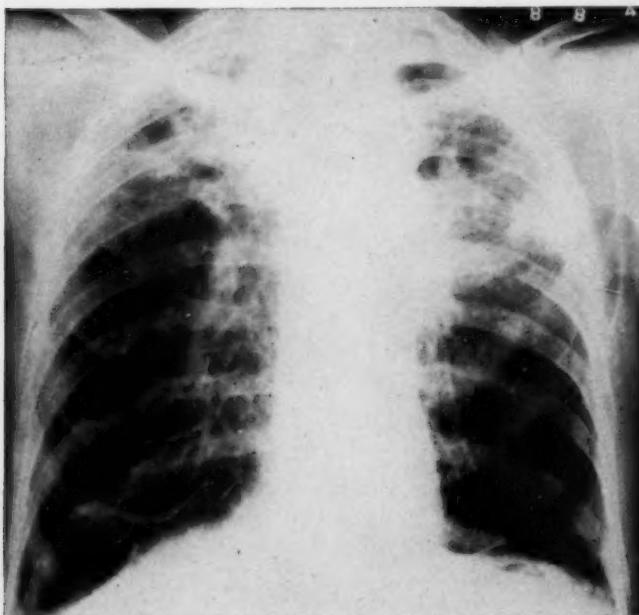


Figure 4. Case 4, August 8, 1949, 2 years later. Marked spread of disease in both upper lungs with cavitation and pleurisy. Some clearing in the left base.

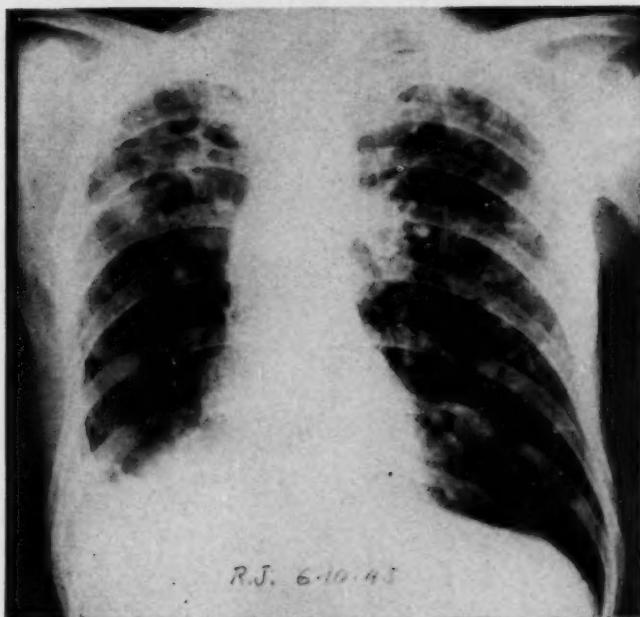


Figure 5. Case 5, June 10, 1943. Scattered infiltrations in both lung fields with probable cavitation in the right first interspace, pleurisy in the right base and mediastinal shift to the right. Note calcifications in the left hilum.

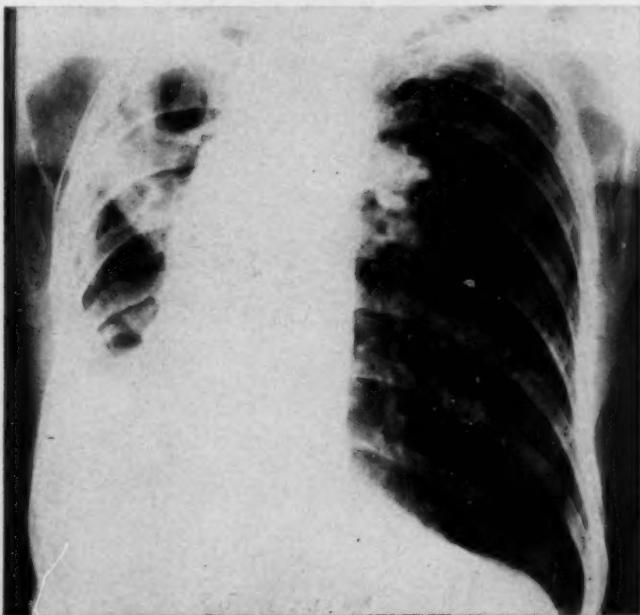


Figure 6. Case 5, November 23, 1948,  $5\frac{1}{2}$  years later. Marked progression of destructive disease in the right, with giant cavity and further retraction of mediastinum. Clearing in the left with scattered calcifications, emphysema and residual pleuritic changes.

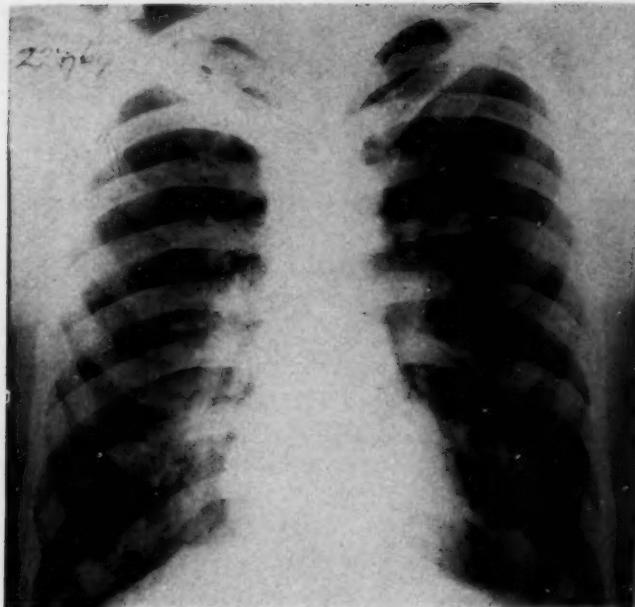


Figure 7. Case 6, June 14, 1947. Infiltration in right hilum extending into right base.

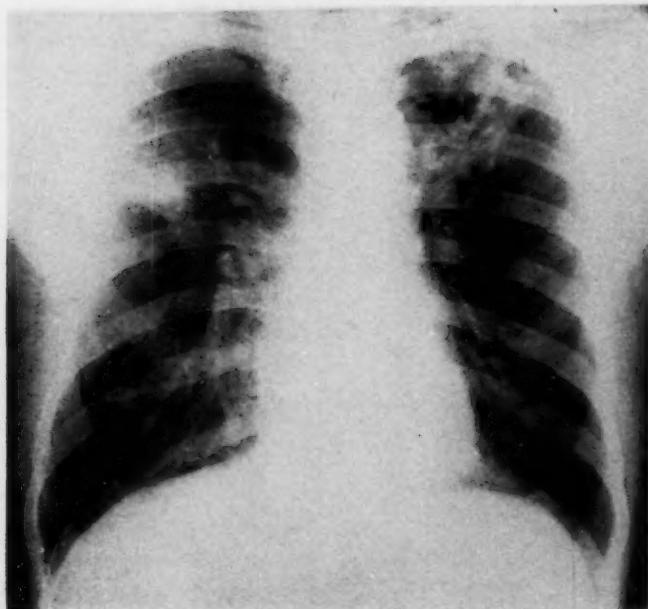


Figure 8. Case 7, March 15, 1945. Infiltration in right second interspace and left upper lobe with question of cavity in the left apex.



Figure 9. Case 7, June 13, 1947, 2 years later. Nodular type of lesions throughout both lung fields with marked spread in the right lower mid-lung field.

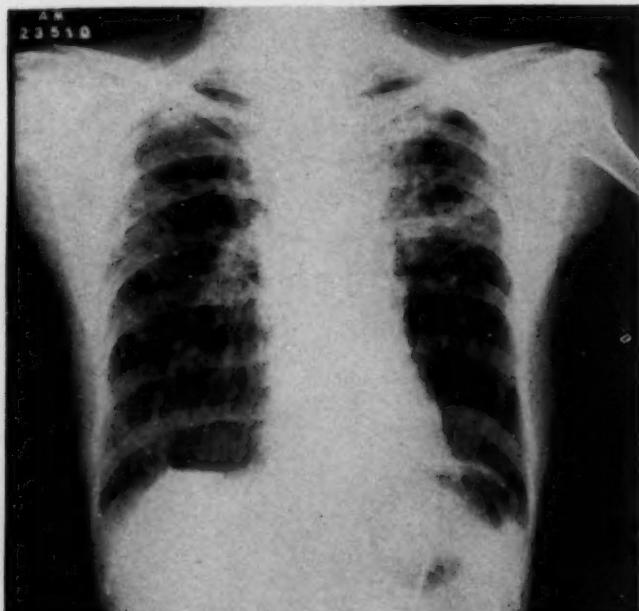


Figure 10. Case 8, July 22, 1947. Infiltrations in both lung fields, more marked on the left. Note calcification in right upper hilum.

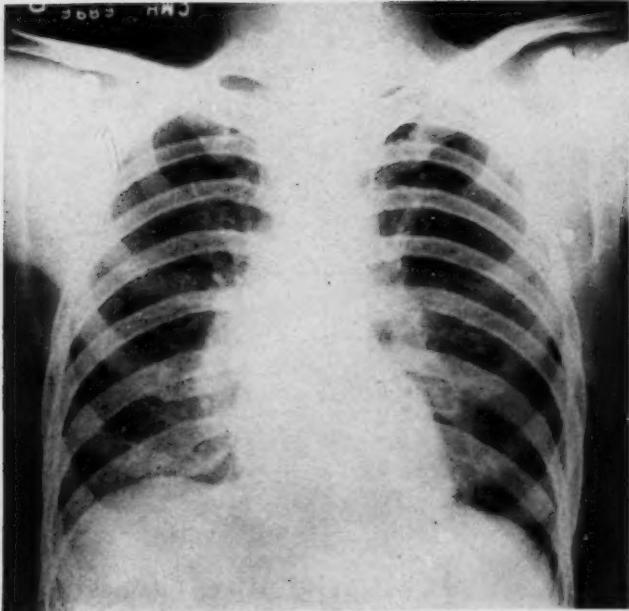


Figure 11. Case 10, November 3, 1947. Generalized fine "granular" lesions, more dense in the perihilar areas with fewer lesions in peripheral lung fields.

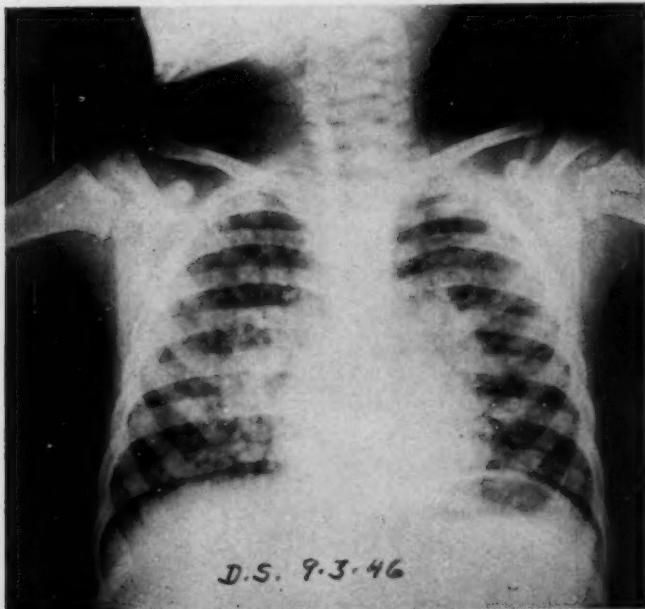


Figure 12. Case 11, September 3, 1946. Miliary infiltrations throughout entire chest with enlargement of hilar nodes bilaterally.

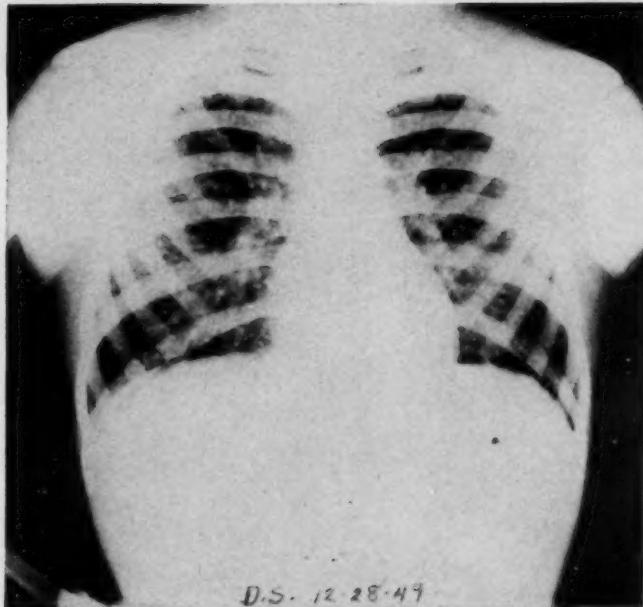


Figure 13. Case 11, December 28, 1949, 3 years later. Small miliary calcified areas throughout the lung fields. Note possible early calcification in the hilar nodes (cf. fig. 2).

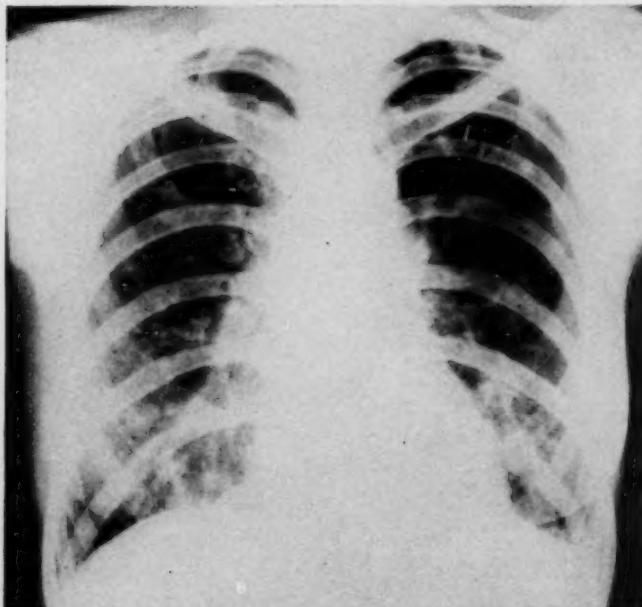


Figure 14. Case 12, April 1, 1949. Soft, ill-defined infiltrates in both lungs with pleurisy in the left base.

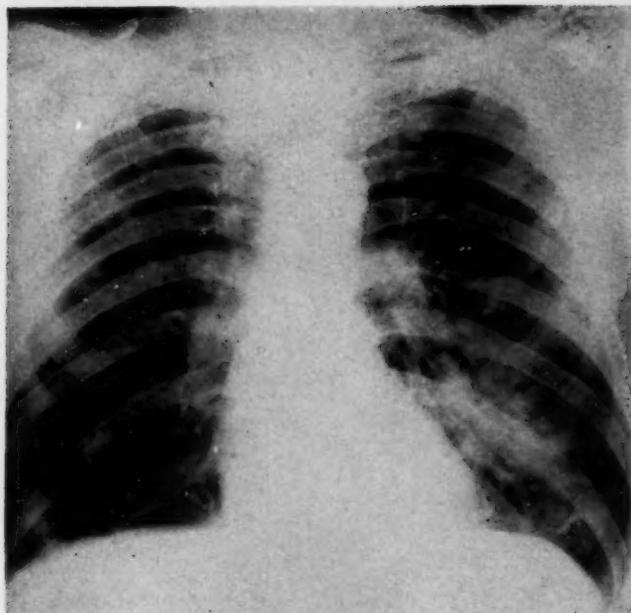


Figure 15. Case 13, September 6, 1949. Infiltration in the left hilar area extending into the mid and lower lung field and left base.

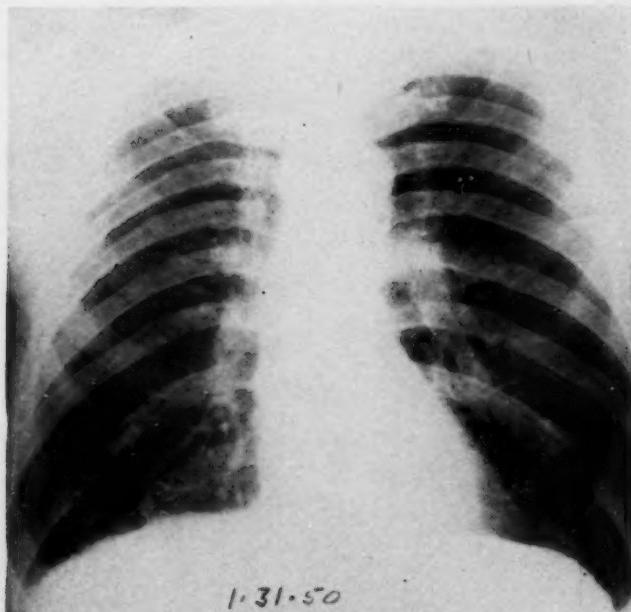
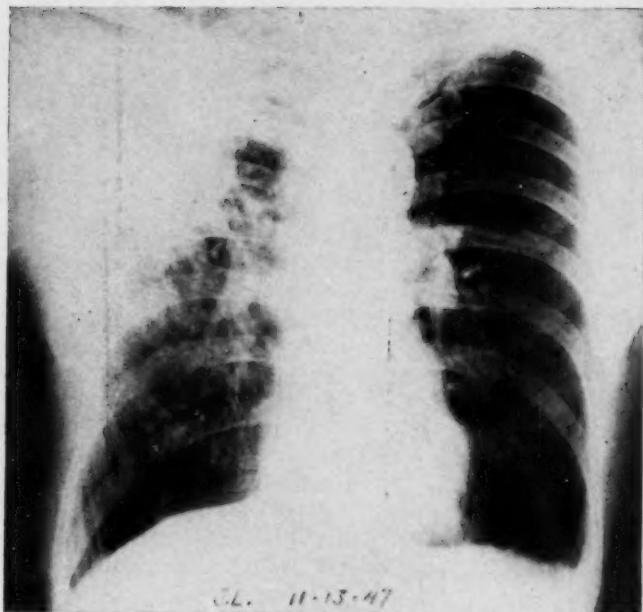
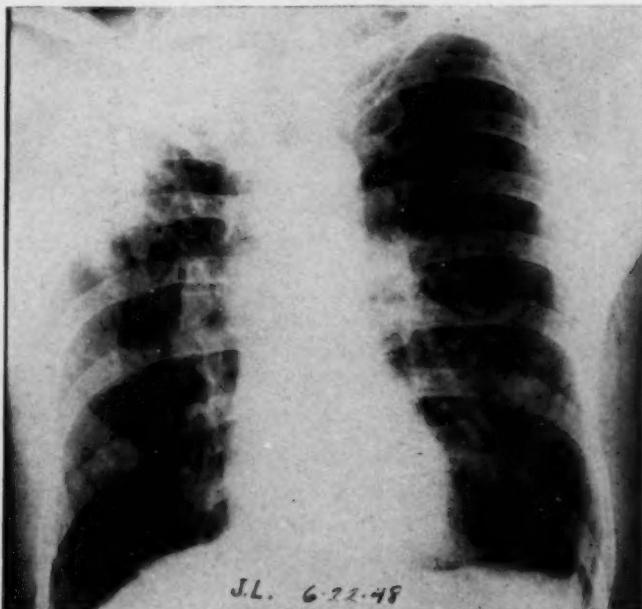


Figure 16. Case 13, January 31, 1950, 4 months later. Marked clearing in the left lower lobe.



J.L. 11-13-47

Figure 17. Case 15, November 13, 1947. Dense infiltration in lateral portion of right upper chest with areas suggestive of cavitation. Early infiltrates in the left mid lung field with old pleuritic changes in the base.



J.L. 6-22-48

Figure 18. Case 15, June 22, 1948, 8 months later. Essentially no change in the right upper with probable cavitation still present. New infiltrations in the left hilum and lower mid-lung field and the right base.

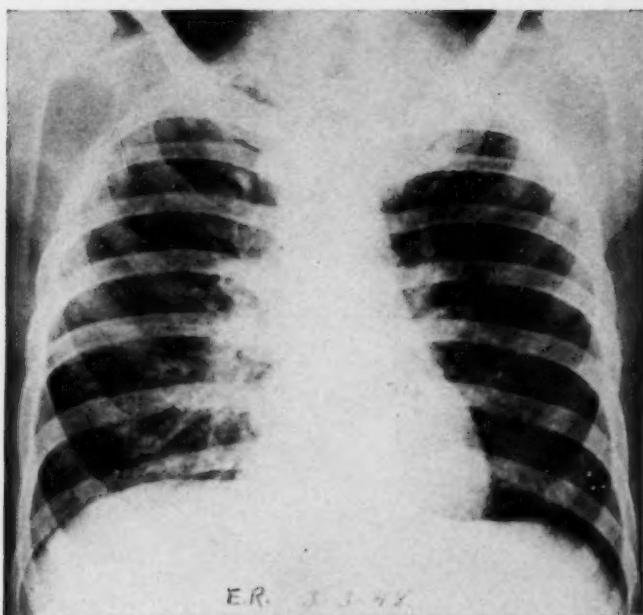


Figure 19. Case 16, March 3, 1948. Multiple soft infiltrates throughout both lung fields, more marked in the right upper.

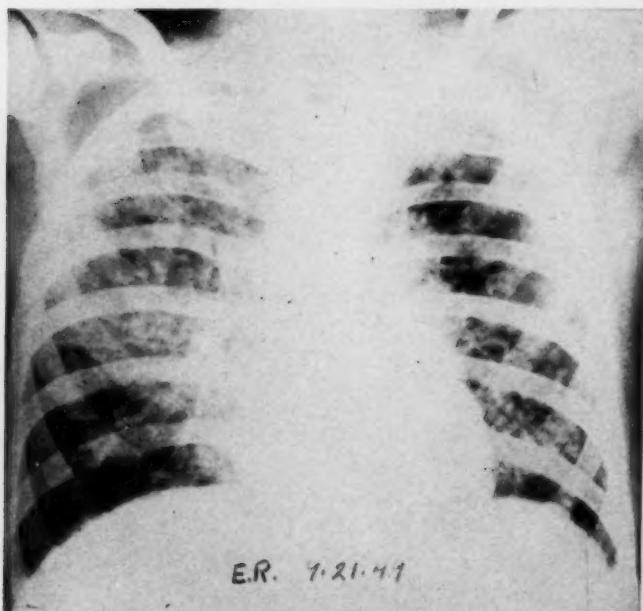


Figure 20. Case 16, September 21, 1949, 1½ years later. Marked increase in disease bilaterally with coalescence of infiltrates in the right upper and widespread scattered infiltrates in the entire left lung.

*History.* The patient's complaints were limited to progressive loss of vision, which had begun in the right eye and had gradually become worse during the previous 12 to 14 years. About 12 years before admission he had had an operation for cataract removal from the right eye without improvement in his vision.

Since the operation, vision in the left eye had gradually failed. Patient had lost his left leg in an accident at 19 years of age and gave a vague history of "heart trouble" beginning 3 years before admission. He entered the hospital for cataract removal.

*Admission findings.* October 10, 1947. The right pupil was grossly distorted and there was an opacity in the left. Breath sounds were distant. There were no other significant findings. Blood pressure was 120/68 and temperature was 99°. The red blood count was not reported, but hemoglobin was 79 percent, and the white blood count was 8,700 per cu. mm. with differential not reported. The blood sedimentation rate was 30 mm. in 1 hour. Routine admission chest X-rays (fig. 17) showed dense infiltration in the right upper lung peripherally, and possible cavitation. The X-ray impression was far-advanced tuberculosis.

*Skin tests.* Tuberculin test was negative on the 19th hospital day, and the histoplasmin test was positive. Similar results were obtained on repeat tests 1 week later. Blastomycin test was negative at this time. Repeat tuberculin and histoplasmin tests at 5 and 7 months after admission gave similar results.

*Complement fixation tests.* A suspicious (+++) complement fixation test for histoplasmosis was found on the 20th hospital day. Similar results were found 1 and 5 months later, while positive (++++) fixation was obtained in the 8th, 11th, and 13th months after admission.

*Mycology and bacteriology.* Five gastric specimens were negative for tuberculosis by culture. Three of seven gastric specimens secured over a period of 5 months, as well as the only sputum specimen obtained, were positive for *H. capsulatum*. The first positive was obtained from the gastric specimen of April 4, 1948. Eight mice injected with gastric specimens were negative, as was a single blood culture.

*Course.* The cataract in the left eye was removed on November 6, 1947, and the postoperative course was uneventful. Patient ran a low-grade fever (99°-100°) during his hospital stay of 53 days, but had no other symptoms. Chest X-rays June 22, 1948, showed essentially the same dense, infiltration in the right upper field with a suggestion of cavitation, as had previously been noted, increased densities in the right base, and an acute infiltration in the left hilum spreading into the lower mid-lung field (fig. 18). He was discharged on December 10, 1947, to be followed in the clinic. The patient had several "heart attacks" after he left the hospital and suddenly expired during one of these attacks on November 16, 1948. The attending physician listed heart disease as the cause of death. An autopsy was not obtained.

*Comment.* The chest lesions in this patient appeared to be of long standing. Yet there were no symptoms referable to the pulmonary disease. Because of the negative tuberculin and positive histoplasmin skin reactions, complement fixation tests were run with suspicious results at first, and positive findings later. Gastric and sputum cultures were positive for *H. capsulatum*, and tubercle bacilli were absent, so that the diagnosis of histoplasmosis appears confirmed. In this case, however, histoplasmosis appeared as a complicating factor, rather than the cause of symptoms or death.

## **Severe Clinical Illness with Death Due to Other Causes**

CASE 16. E. R., white male, 32 years old. Patient was employed as an engineer and had travelled about the country extensively. He had lived in Iowa for 18 years and, for 9 years prior to admission, in a small city in central Kansas. He was studied because he had had a diagnosis of torulosis (cryptococcosis) which had been made at another hospital.

**History.** The patient's symptoms were chills, fever, weight loss, draining left supraclavicular lymph nodes, and arthritis. His illness had begun 1½ years before admission when he had developed painful, swollen, raised areas on his shins; these had disappeared after penicillin therapy. Three months later, painful migratory swellings of the knees and ankles had appeared and these had been relieved by gold therapy. Thirteen months before admission, the arthritis had recurred without relief by further gold therapy. Five months later an evening temperature rise of 3° had been noted, with weight loss, malaise, irregular chills, and sweats. Fever had persisted, and 6 months before admission the patient had been studied by a clinic where a diagnosis of rheumatic fever was made. Bed rest with salicylates was advised. One month later cyanosis of the left arm developed, which was diagnosed as thrombophlebitis. This was accompanied by fever (up to 103°) which persisted in spite of sulfa drugs, streptomycin and penicillin. The cyanosis disappeared, but the fever persisted and a firm, nontender left cervical lymph node was noted in December 1947. A diagnosis of Hodgkins' disease was made, and the patient entered the Mayo Clinic. Here, the tuberculin test was negative, but biopsy of the enlarged cervical node was reported as suspicious of tuberculosis. An atypical acid-fast organism was isolated repeatedly from the sputum, but it was nonpathogenic for animals. *Torula* (cryptococci) were repeatedly isolated from the patient's sputum. Multiple infiltrations were noted in the lungs, and review of the older X-ray films revealed that the same infiltration had been present at least 3 months earlier. The white blood count varied from 14,000 to 25,000 per cu. mm. with predominance of polymorphonuclear leukocytes. The patient was transferred with the tentative diagnosis of tuberculosis and torulosis.

**Admission findings.** February 25, 1948. The patient was well developed but poorly nourished, and looked both acutely and chronically ill. He had a respiratory rate of 28 per minute, a draining sinus in the left supraclavicular region, and rheumatoid deformities of his fingers. Blood pressure was 100/70, and pulse 100. Red blood count was 4,100,000 per cu. mm with 64 percent hemoglobin; white blood count was 22,000 with 91 percent polymorphonuclear leukocytes, 8 lymphocytes, and 1 monocyte. Urine showed a faint trace of albumin and 3 to 4 white cells per high power field. Blood chemistry was within normal limits. X-rays showed multiple poorly circumscribed infiltrations scattered throughout both lung fields (fig. 19).

**Skin tests.** Tuberculin and histoplasmin tests were positive on admission, while a blastomycin test was doubtful and coccidioidin, negative. Three repeat tests showed essentially the same results except that blastomycin tests were negative in three applications. One trichinosis skin test was negative.

**Complement fixation tests.** Serum gave a positive (++++) complement fixation twice during the first week, and three additional times during the first month. The same findings were observed for 5 months. The reaction fell to suspicious (++) during the 7th month and continued so through the 10th month. Eleven subsequent sera were negative or at most doubtful (++) until death, with the exception of one positive (++++) recorded 2 months before death.

**Mycology and bacteriology.** Thirteen sputa, seven gastric specimens, two blood

cultures, three cultures from the neck or psoas abscesses and one urine were negative for acid-fast organisms by culture although several colonies of atypical acid-fast organisms were found. These are apparently nonpathogenic in guinea pigs. Four guinea pigs inoculated with these specimens were negative. Nineteen sputa, 11 gastric specimens, 4 specimens from neck or psoas abscesses, 4 blood samples, and 1 urine were negative for *H. capsulatum* on culture, with the exception of 1 positive sputum. Twenty-one mice inoculated with these materials were negative on autopsy, and organs were also negative on culture. In addition, 25 stool cultures were negative. At autopsy, cultures were made from the spleen, liver, lung, kidney, psoas abscess, and periaortic node, but all were negative for tuberculosis and fungi. Eight mice were inoculated with pooled tissue and were negative. Three guinea pigs were also inoculated and were negative at autopsy, except for an atypical acid-fast organism isolated from one pig.

**Course.** During the first 8 months of hospitalization, the patient had a daily temperature of 100° to 102°; during the next 5 months, temperatures fell gradually and rarely exceeded 99° during the later months. Patient remained essentially afebrile for the next 6 months, except for one period of 8 days during which the temperature exceeded 99°, reaching 102° on one day. During all this period, there was no change in the chest X-ray picture. The patient had a persistent leukocytosis ranging from 17,000 to 25,000 white blood cells per cu. mm. with the polymorphonuclear leukocytes ranging from 82 to 97 percent. An increase in the eosinophils was also found, and at one time these reached 15 percent.

Because of the persistent leukocytosis, careful X-ray studies were performed, revealing a psoas abscess on the left on August 1, 1949. Urea clearance and PSP showed only about 50 percent normal function. On August 10, the psoas abscess was explored and 300 cc. of pus evacuated. Following surgery, the patient gradually developed urinary failure and died on October 12, 1949 of urinary retention with a blood-NPN of over 130. Chest X-rays taken during the last month of life (September 21, 1949) revealed marked increase in the amount of infiltration, possibly more dense on the right, with coalescence of some lesions (fig. 20).

**Autopsy findings.** Acute glomerulonephritis with ascending suppurative pyelonephritis, superimposed on diffuse granulomatosis involving lungs, liver, kidneys, psoas muscles, spleen, lymph nodes, and myocardium. Extensive periarteritis was also found, especially of the pancreas, leading to the diagnosis of periarteritis nodosa. The granuloma resembled Hodgkins' type in some places, while in others it suggested mycotic granuloma, but was not typical of tuberculosis. No acid-fast or other type organisms were seen.

**Comment.** This case still remains a diagnostic problem as the pathological changes found on autopsy were not typical of any one specific disease. It is known that granulomatous disease may be caused by various types of fungi, among other things, and it is possible that in this case the atypical acid-fast organism which was repeatedly isolated may have had an etiologic relationship to the lesions found. Since periarteritis nodosa and Hodgkins' disease still pose etiologic problems, the multiple diagnosis made at autopsy suggests some interesting speculations concerning the possible relationship between all these granulomas, including those shown to be mycotic in origin. The single sputum culture found to be positive for *H. capsulatum* certainly does not serve to explain the entire disease picture. However,

the role which this fungus may have played in the over-all picture of diffuse granuloma remains obscure.

### Discussion and Summary

The present paper reports on six new patients from whom *H. capsulatum* was recovered and adds material on the ten previously reported from the Kansas City area. Two of the six newly reported patients have recovered; one is still ill, and three are dead.

All of the six new patients showed negative skin reactions to blastomycin and four of them were negative to coccidioidin. (Cases 11 and 15 were not tested.) Three of the six showed disseminated lesions on chest X-rays: one (case 11) healed with the development of miliary calcification; the second (case 12) healed with disappearance of the lesions; and in the third (case 16) the lesions persisted unchanged for 2 years before the patient died of causes other than histoplasmosis.

No cases of coexistent tuberculosis and histoplasmosis were found among these six new patients although two were found in the original ten cases. Two of the six had laryngeal histoplasmosis. One of the six was diagnosed as having preexisting torulosis (cryptococcosis) and died of periarteritis nodosa and multiple granuloma of undetermined etiology.

### Clinical and Laboratory

Case	First observed	Skin tests			Complement fixation		Mycology and bacteriology	
		Date	Histo	Tbcln			Date	Specimen
1. Male 13 years-----	2- 5-45	2- 5-45	neg.		8-18-47	neg.	11-23-45	gast.
		6- 7-45	pos.		9-15-47	pos.	11-24-45	gast.
		11-26-45	pos.	neg.	9-17-47	pos.	11-25-45	gast.
		1- 4-46	pos.	neg.	6-10-48	to 5 susp.	11-23-45	
		6- 4-46	pos.	neg.	12-9-49		(11-25-45)	gast.
		10- 4-48	pos.	neg.			1- 9-46	
2. Male 5 months-----	3- 1-47	3- 2-47	neg.	neg.	6-30-47	pos.	3-18-47	blood.
		4-16-47	pos.	neg.	7-10-47	pos.	3-21-47	blood.
		5- 7-47	pos.	neg.	8-15-47	pos.	3-21-47	marrow
		7-26-47	pos.	neg.	9-29-47	susp.	4- 8-47	8 blood.
		9- 8-47	pos.	neg.	10-27-47	pos.	8-19-47	
		11- 5-48	pos.	neg.	11-10-47	pos.		
					2-18-48	susp.		
					5-20-48	pos.		
					6-27-49	susp.		
					1-16-50	neg.		
3. Female 20 months-----	3-23-47	3-24-47	neg.	neg.	9- 4-47	susp.	8-19-47	spleen.
		8-25-47	pos.	neg.	9-11-47	pos.	8-19-47	spleen.
		9- 2-47	pos.		10-13-47	pos.	9- 2-47	gast.
		8-16-49	pos.	neg.	12- 4-47	pos.	9- 2, 3,	
							5-47	
					10-18-48	neg.	9-3, 5-47	2 gast.
					8-16-49	neg.		
					2-18-50	neg.		

\*Cases 1 to 10 from Pub. Health Rep. 63: 315 (1948), reference No. 4. Cases 11 to 16 are reported in this paper.

The accompanying table presents pertinent clinical and laboratory data on all 16 cases. This case material shows variations in diagnostic certainty ranging from the clear-cut, uncomplicated cases of clinical histoplasmosis, through the probable cases, to those in which the finding of *Histoplasma* was incidental to the diagnosis of another disease. Emphasis should perhaps be placed on the observation that the fungus may be found to be present in a wide variety of clinical conditions. Whether it may play a decisive role as the etiologic agent must be carefully considered in the light of all available evidence pertaining to the disease process. And, perhaps most important of all, one must not only think of histoplasmosis in the differential diagnosis of a granulomatous or infective disease, but painstaking search for the organism must frequently be made in order to establish the correct diagnosis.

Of the 16 cases studied, 5 have recovered. Two other cases are classed as still ill. The fact that almost one-third of cases in our series recovered supports the original concept of Palmer (1) and Christie and Peterson (2) of the occurrence of nonfatal histoplasmosis. This concept is further supported by the reports of nine other proved recovered cases in the literature (5-12).

#### *Findings for 16 Patients\**

Mycology and bacteriology—Continued			Chest X-ray	Status	Additional findings
Test	H. c.	T. b.			
cult. cult. cult.	pos. neg. neg.	neg. neg. neg.	miliary infiltrations 4-10-45. Miliary calcifications 12-9-49.	Living and well 3-23-50.	Recovery uneventful.
g. pig.	pos.	neg.			
17 cult.	neg.				
cult. cult. cult.	neg. pos. pos.	----- ----- -----	Normal 3-15-47. Normal 1-16-50.	Living and well 1-16-50.	3-2-47 typhoid, paratyphoid A and B, brucellosis agglutinations all negative.
8 cult.	8 neg.	-----			
cult. mouse. cult.	pos. pos. pos.	neg. neg. neg.	Infiltration in right lower lobe 7-5-47. Calcification in right lower lobe and hilar node 2-18-50.	Living and well 2-18-50.	8-19-47 surgical specimens of spleen, liver and abdominal lymph node showed multiple granulomatous lesions. H. c. not identified on microscopic sections.
3 mice. 2 cult.	neg. 2 neg.	2 neg.			

\*Cases 1 to 10 from Pub. Health Rep. 63: 315 (1948), reference No. 4. Cases 11 to 16 are reported in this paper.

Clinical and Laboratory

Case	First observed	Skin tests			Complement fixation		Mycology and bacteriology	
		Date	Histo	Tbeln			Date	Specimen
4. Male 52 years-----	10-26-47	10-27-47 1- 5-48 10-26-48	pos. pos. pos.	neg. pos. pos.	10- 8-47 10-23-47 10-28-47 1- 5-48 to 10- 6-49	pos. pos. pos. 10 pos.	10-27-47 10-27-47 10-27-47 10-28-47 10-29-47 10-29-47 12-31-47	spt. past. biopsy. gast. spt. bronch. spt.
5. Male 64 years-----	12- 5-47	12- 6-47 12-17-47 1- 5-48 12- 8-48 12-13-48 4-19-49	pos. pos. pos. pos. pos. pos.	----- pos. pos. pos. pos. neg.	12- 6-47 12-19-47 1- 5-48 to 5- 1-49	pos. pos. 6 pos.	12-11-47 to 4-21-49	25 spt. 5 gast. 3 gast. 1 stool. 9 spt. 3 blood. 7 spt. 2 spt.
6. Male 22 years-----	6-13-47	6-17-47 7- 8-47 7-22-47 8-12-47 9- 3-47	pos. pos. pos. pos. pos.	pos. pos. pos. pos. pos.	7- 5-47 7- 9-47 7-22-47 8-12-47 9- 3-47	neg. pos. doubt. doubt. neg.	7- 8-47 8-14-47 8-15-47 9- 3-47	spt. spt. spt. blood.
Male 48 years-----	5-20-47	5-26-47 7- 2-47 7- 9-47 7-17-47 7-29-47	neg. pos. pos. pos. pos.	neg. neg. neg. neg. neg.	7- 1-47 7- 2-47 7- 8-47 7-16-47	pos. pos. neg. pos.	5-27-47 5-28-47 5-29-47 7- 2-47	gast. gast. gast. spleen.
8. Female 53 years-----	7-14-47	8- 8-47 8-20-47 9- 8-47 9-22-47	neg. neg. neg. neg.	neg. neg. neg. neg.	8- 8-47	neg.	8- 8-47 8-11-47 8-12-47 8-20-47	blood. marrow. bronch. marrow. node. node.
9. Female 6 months-----	10-21-47	10-30-47	neg.	neg.	10-27-47 11- 3-47	susp. susp.	10-30-47 10-31-47 10-31-47 10-31-47	blood. blood. marrow. marrow.
10. Male 37 years-----	10-21-47	11- 5-47	neg.	neg.	11- 5-47	pos.	-----	-----

\*Cases 1 to 10 from Pub. Health Rep. 63: 315 (1949), reference No. 4. Cases 11 to 16 are reported in this paper.

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**Findings for 16 Patients\*—Continued**

Mycology and bacteriology—Continued			Chest X-ray	Status	Additional findings
Test	H. e.	T. b.			
cult. cult. cult. cult. cult. cult. cult. 2 g. pigs 2 mice	pos. neg. neg. neg. neg. pos. neg. pos. pos.	----- neg. neg. neg. neg. neg. neg. neg. neg.	Infiltration of entire left and upper right lobes, 10-23-47. Cavities in upper left and upper right lobes 8-8-49.	Slowly progressive disease 4-12-50.	13 sputum specimens cultured 1-15-48 to 12-6-48: 8 positive and 4 negative for H. e., 8 negative for T. b. Animal inoculations of 3 divided specimens: 2 of 7 mice and 1 of 7 rats positive for H. e.; 3 guinea pigs negative for T. b.
40 cult. 7 cult. 6 mice. cult. 10 mice. 3 cult. 4 g. pigs. 6 rats.	{13 pos. 7 neg. {1 pos. 12 neg. {1 pos. 15 neg. 1 neg. {4 pos. 6 neg. neg. 6 pos.	{20 neg. {4 neg. ----- ----- 4 neg.	Infiltration in right upper lobe, 6-10-43. Cavities in right lung; fibrosis and calcification in left lung 11-23-48.	Died 5-1-49.	Sections of lung, spleen and adrenals morphologically positive for H. e. Pooled organ cultures, rat and guinea pig inoculations negative for H. e. and T. b. Spleen culture positive, rat inoculation for H. e. negative. Cultures and animal inoculations from lung and adrenals all negative for H. e. and T. b.
cult. cult. cult. cult.	neg. neg. neg. neg.	neg. neg. neg. neg.	Increased markings right lower lung 6-14-47.	Died 9-10-47.	Autopsy diagnosis: pulmonary histoplasmosis, chronic pneumonia and chronic nephritis. H. e. identified in lung sections. Pooled organ cultures negative for H. e. and T. b.; 2 guinea pigs positive for T. b., 1 of 3 mice positive for H. e.
cult. (g. pig. cult. (g. pig. cult. (g. pig. cult. (section.	neg. neg. neg. neg. pos. neg. pos.	neg. neg. neg. neg. neg. neg. neg.	Infiltrations in right and left lungs with cavity in the left, 3-15-45. New infiltration in right mid-lung field 6-13-47.	Died 9-8-47.	Autopsy: Pooled organ culture positive for H. e.; lung culture and guinea pig positive for both H. e. and T. b.; adrenal culture contaminated; guinea pig positive for both H. e. and T. b.
cult. cult. cult. cult. cult. section.	neg. neg. neg. neg. neg. neg.	----- ----- ----- ----- ----- -----	Infiltration and fibrosis in both upper lung fields 7-22-47.	Died 10-12-47.	Autopsy diagnoses: Hodgkins disease and histoplasmosis. Pooled organ cultures positive for H. e., negative for T. b.; liver and spleen pooled culture positive for H. e.; lung and lymph node pooled culture negative for H. e. and negative for T. b. Liver and adrenal sections positive morphologically for H. e.
cult. cult. smear. cult.	pos. pos. pos. pos.	----- ----- ----- -----	Infiltration in right lower lobe 10-21-47.	Died 11-3-47.	Autopsy diagnosis: histoplasmosis. Pooled organ culture, 2 of 4 mice and 1 of 3 guinea pigs positive for H. e.; all 3 negative for T. b. Spleen, blood, marrow smears, blood culture and tissue section of organs positive for H. e.
			Diffuse granular infiltrations 11-3-47.	Died 11-7-47.	Autopsy diagnosis: generalized histoplasmosis. Tissue sections of lung, liver, spleen, lymph node positive for H. e.

\*Cases 1 to 10 from Pub. Health Rep. 63: 315 (1948), reference No. 4. Cases 11 to 16 are reported in this paper.

Case	First observed	Skin tests			Complement fixation		Mycology and bacteriology	
		Date	Histo	Tbeln			Date	Specimen
4. Male 52 years.....	10-26-47	10-27-47 1-5-48 10-26-48	pos. pos. pos.	neg. pos. pos.	10-8-47 10-23-47 10-28-47 1-5-48 to 10-6-49	pos. pos. pos. 10 pos.	10-27-47 10-27-47 10-27-47 10-28-47 10-29-47 10-29-47 12-31-47	spt. gast. biopsy. gast. spt. bronch. spt.
5. Male 64 years.....	12-5-47	12-6-47 12-17-47 1-5-48 12-8-48 12-13-48 4-19-49	pos. pos. pos. pos. pos. pos.	..... pos. pos. pos. pos. neg.	12-6-47 12-19-47 1-5-48 to 5-1-49	pos. pos. 6 pos.	12-11-47 to 4-21-49	25 spt. 5 gast. 3 gast. 1 stool. 9 spt. 3 blood. 7 spt. 2 spt.
6. Male 22 years.....	6-13-47	6-17-47 7-8-47 7-22-47 8-12-47 9-3-47	pos. pos. pos. pos. pos.	pos. pos. pos. pos. pos.	7-5-47 7-9-47 7-22-47 8-12-47 9-3-47	neg. pos. doubt. doubt. neg.	7-8-47 8-14-47 8-15-47 9-3-47	spt. spt. spt. blood.
Male 48 years.....	5-20-47	5-26-47 7-9-47 7-17-47 7-29-47	neg. pos. pos. pos.	neg. neg. pos. pos.	7-1-47 7-2-47 7-8-47 7-16-47	pos. pos. neg. pos.	5-27-47 5-28-47 5-29-47 7-2-47	gast. gast. gast. spleen.
8. Female 53 years.....	7-14-47	8-8-47 8-20-47 9-8-47 9-22-47	neg. neg. neg. neg.	neg. neg. neg. neg.	8-8-47	neg.	8-8-47 8-11-47 8-12-47 8-20-47	(blood. marrow. bronch. marrow. node. node.)
9. Female 6 months....	10-21-47	10-30-47	neg.	neg.	10-27-47 11-3-47	susp. susp.	10-30-47 10-31-47 10-31-47 10-31-47	blood. blood. marrow. marrow.
10. Male 37 years.....	10-21-47	11-5-47	neg.	neg.	11-5-47	pos.	.....	.....

\*Cases 1 to 10 from Pub. Health Rep. 63: 315 (1949), reference No. 4. Cases 11 to 16 are reported in this paper.

*ov*  
Findings for 16 Patients\*—Continued

Mycology and bacteriology—Continued			Chest X-ray	Status	Additional findings
Test	H. c.	T. b.			
cult. cult. cult. cult. cult. cult. cult. cult. 2 g. pigs 2 mice	pos. neg. neg. neg. neg. pos. neg. pos. neg. pos. pos.	neg. neg. neg. neg. neg. neg. neg. neg. neg. neg.	Infiltration of entire left and upper right lobes, 10-23-47. Cavities in upper left and upper right lobes 8-8-49.	Slowly progressive disease 4-12-50.	13 sputum specimens cultured 1-15-48 to 12-6-48; 8 positive and 4 negative for H. c., 8 negative for T. b. Animal inoculations of 3 divided specimens: 2 of 7 mice and 1 of 7 rats positive for H. c.; 3 guinea pigs negative for T. b.
40 cult. 7 cult. 6 mice. cult. 10 mice. 3 cult. 4 g. pigs. 6 rats.	{ 13 pos. { 7 neg. { 1 pos. { 2 neg. { 1 pos. { 5 neg. 1 neg. { 4 pos. { 6 neg. neg. 6 pos.	{ 20 neg. { 4 neg. { 1 neg. { 4 neg. { 4 neg. neg. neg. neg. neg. neg. neg.	Infiltration in right upper lobe, 6-10-43. Cavities in right lung; fibrosis and calcification in left lung 11-23-48.	Died 5-1-49.	Sections of lung, spleen and adrenals morphologically positive for H. c. Pooled organ cultures, rat and guinea pig inoculations negative for H. c. and T. b. Spleen culture positive, rat inoculation for H. c. negative. Cultures and animal inoculations from lung and adrenals all negative for H. c. and T. b.
cult. cult. cult. cult.	neg. neg. neg. neg.	neg. neg. neg. neg.	Increased markings right lower lung 6-14-47.	Died 9-10-47.	Autopsy diagnosis: pulmonary histoplasmosis, chronic pneumonia and chronic nephritis. H. c. identified in lung sections. Pooled organ cultures negative for H. c. and T. b.; 2 guinea pigs positive for T. b., 1 of 3 mice positive for H. c.
cult. tg. pig. cult. tg. pig. cult. tg. pig. cult. (section.)	neg. neg. neg. neg. pos. neg. pos. pos.	neg. neg. neg. neg. neg. neg. neg. neg.	Infiltrations in right and left lungs with cavity in the left, 3-15-45. New infiltration in right mid-lung field 6-13-47.	Died 9-8-47.	Autopsy: Pooled organ culture positive for H. c.; lung culture and guinea pig positive for both H. c. and T. b.; adrenal culture contaminated; guinea pig positive for both H. c. and T. b.
cult. cult. cult. cult. cult. section.	neg. neg. neg. neg. neg. neg.	neg. neg. neg. neg. neg. neg.	Infiltration and fibrosis in both upper lung fields 7-22-47.	Died 10-12-47.	Autopsy diagnoses: Hodgkins disease and histoplasmosis. Pooled organ cultures positive for H. c., negative for T. b.; liver and spleen pooled culture positive for H. c.; lung and lymph node pooled culture negative for H. c. and negative for T. b. Liver and adrenal sections positive morphologically for H. c.
cult. cult. smear. cult.	pos. pos. pos. pos.	neg. neg. neg. neg.	Infiltration in right lower lobe 10-21-47.	Died 11-3-47.	Autopsy diagnosis: histoplasmosis. Pooled organ culture, 2 of 4 mice and 1 of 3 guinea pigs positive for H. c.; all 3 negative for T. b. Spleen, blood, marrow smears, blood culture and tissue section of organs positive for H. c.
			Diffuse granular infiltrations 11-3-47.	Died 11-7-47.	Autopsy diagnosis: generalized histoplasmosis. Tissue sections of lung, liver, spleen, lymph node positive for H. c.

\*Cases 1 to 10 from Pub. Health Rep. 63: 315 (1948), reference No. 4. Cases 11 to 16 are reported in this paper.

Clinical and Laboratory

Case	First observed	Skin tests			Complement fixation		Mycology and bacteriology	
		Date	Histo	TbcIn			Date	Specimen
11. Male 4 years.....	9-11-46	8-25-46 9-11-46 10-17-46 12- 3-46 4-22-47 8-12-47	doubt. pos. pos. pos. neg. pos.	neg. neg. neg. neg. neg. neg.	8-12-47 1-21-48 4- 7-48 11-16-48 4-29-49 12-28-49	pos. pos. pos. pos. pos. susp.	9-12-46 9-12-46 9-13-46 9-13-46 9-17-46 9-16-46 10-17-46 to 10-19-46 1-29-48	blood. gast. marrow. 5 gast. blood. 4 gast. tonsil.
12. Female 41 years.....	4- 1-49	{ 4-16-49 5-16-49	pos. pos.	pos. pos.	4- 7-49 4-19-49 5-17-49 6-29-49 7-15-49 9-21-49 2-12-50	pos. pos. susp. susp. susp. pos. susp.	4- 2-49 4- 7-49 5-17-49 5-19-49	spt. spt. spt. spt.
13. Male 64 years.....	9- 6-49	11-14-49 12- 7-49 1- 9-50	pos. pos. pos.	neg. neg. neg.	11-17-49 to 12-28-49	{ pos. 4 susp.	{ 11- 9-49 to 12-28-49	16 spt.
14. Male 69 years.	12-13-49	11-13-49 12-13-49	pos. pos.	neg. neg.	11-16-49 12-13-49 12-16-49 12-18-49 12-20-49	pos. pos. pos. pos. pos.	12-14-49 to 12-23-49	22 spt.
15. Male 61 years.	10-10-47	10-29-47 11- 4-47 3-22-48 5-10-48	pos. pos. pos. pos.	neg. neg. neg. neg.	10-30-47 11-10-47 3-22-48 6-23-48 9-23-48 11- 5-48	susp. susp. susp. pos. pos. pos.	10-29-47 to 11-18-48 11-26-47 12-10-47 4- 5-48 4- 6-48 4- 7-48	5 gast. 2 gast. blood. gast. gast. gast. spt.
16. Male 32 years.	2-25-48	2-28-48 3- 1-48 10-26-48 5-25-49 9-26-49	----- pos. pos. pos. doubt.	pos. pos. pos. pos.	3- 1-48 to 8-13-48 10-25-48 to 1-24-49 2-16-49 7-14-49 8-11-49 9-26-49	{ 8 pos. 3 susp. 7 neg. 3 susp. pos. neg.	3- 3-48 to 9-29-49 3-23-48 to 9-29-49 4-23-48 3-31-48 to 8-18-48	18 spt. 6 blood. spt. 11 gast.

\*Cases 1 to 10 from Pub. Health Rep. 63: 315 (1948), reference No. 4. Cases 11 to 16 are reported in this paper.

*Findings for 16 Patients\**—Continued

Mycology and bacteriology—Continued			Chest X-ray	Status	Additional findings
Test	H. c.	T. b.			
cult. cult. cult. (10 cult. (1 hamst. cult. 4 cult. (1 cult. (4 mice.	neg. neg. neg. 5 neg. neg. neg. pos. neg.	----- neg. ----- 5 neg. ----- neg. ----- neg.	Miliary infiltration 9-3-46. Miliary calcification 12-28-49.	Living and well 12-28-49.	Tonsil sections showed granuloma but H.c. not identified in sections.
cult. cult. cult. cult.	pos. neg.	neg.	Scattered infiltrations bilaterally 4-1-49. Clear chest 12-8-49.	Living and well 3-3-50.	Tuleremia, typhoid, and brucellosis agglutinations negative 3-25-49 and 4-12-49. Migratory allergic arthritis 4-20-49 and generalized rash 4-27-49, probably drug sensitivity.
{19 cult. (15 mice. g. pig.	{9 pos. {6 neg. {5 pos. {10 neg.	4 neg. ----- neg.	Infiltration in left lower lobe 9-6-49. Marked clearing in left lower lobe 1-31-50.	Discharged improved from hospital 3-9-50; still improving when last seen on 4-11-50.	Laryngeal biopsies 9-26-49, 11-3-49 and 1-4-50; acute and chronic granulation tissue with H.c. in mononuclear and giant cells.
{28 cult. (6 mice. g. pig.	{20 pos. {2 neg. {4 pos. {2 neg.	{6 neg. ----- neg.	Generalized bilateral granularity 11-10-49. Granularity in right upper lobe 12-13-49.	Died 12-27-49.	Laryngeal biopsy 11-18-49: positive histologically for H. c. Autopsy diagnosis: generalized histoplasmosis, chronic femoral phlebitis with terminal pulmonary embolus. Lung, blood, brain, adrenal, liver, heart, spleen and larynx cultures positive for H. c.; pooled organ inoculation of 2 mice positive for H. c.; 2 cultures and 2 guinea pigs negative for T. b.
8 cult. 4 mice. cult. (2 mice. (cult. (cult. (2 mice. cult. cult. cult.	3 neg. 4 neg. neg. neg. neg. pos. neg. pos. pos.	5 neg. ----- ----- ----- ----- ----- ----- ----- ----- -----	Infiltration in right upper lobe with cavity 11-13-47. No change on film of 6-22-48.	Died 11-16-48.	No autopsy. Death due to "heart attack."
{31 cult. (6 mice. 6 cult. cult. 11 cult. 11 mice. 3 g. pigs.	18 neg. 6 neg. neg. pos. 11 neg. 11 neg. 3 neg.	13 neg. ----- ----- ----- 7 neg. 3 neg.	Scattered soft infiltrates 3-3-49. Disseminated and coalescent infiltrates 9-21-49.	Died 10-12-49.	Atypical acid-fast organisms cultured from sputum 3-10-48, from an abscess 8-6-48 and from 1 of 3 guinea pigs inoculated with pooled autopsy organs. Autopsy diagnosis: periarthritis nodosum and granulomatosis of unknown etiology. Cultures and animal inoculations of autopsy tissues all negative for H. c. and T. b.

\*Cases 1 to 10 from Pub. Health Rep. 63:315 (1948), reference No. 4. Cases 11 to 16 are reported in this paper.

## ACKNOWLEDGMENT

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## Incidence of Disease

*No health department, State or local, can effectively prevent or control disease without knowledge of when, where, and under what conditions cases are occurring*

### UNITED STATES

#### Reports From States for Week Ended July 15, 1950

New cases of acute poliomyelitis reported in the Nation for the current week numbered 665, an increase over the 478 cases reported for the preceding week. However, the number was lower than the 1,014 cases reported for the corresponding period last year. The cumulative total (3,194) for the current "disease" year was below the corresponding total of 3,968 for last year, the highest year on record. The "disease" year for acute poliomyelitis begins with the twelfth week of the calendar year.

For the current week, all geographic divisions showed increases over the preceding week. These increases ranged from 4 cases reported in the Mountain States to 34 cases each in the East North

#### Comparative Data for Cases of Specified Reportable Diseases: United States

[Numbers after diseases are International List numbers, 1948 revision]

Disease	Total for week ended—		5-year median 1945-49	Seasonal low week	Cumulative total since seasonal low week		5-year median 1944-45 through 1948-49	Cumulative total for calendar year		5-year median 1945-49
	July 15, 1950	July 16, 1949			1949-50	1948-49		1950	1949	
Anthrax (062)	1	(1)	(1)	(1)	(1)	(1)	(1)	26	23	(1)
Diphtheria (055)	60	84	138	27th	60	84	138	3,188	3,852	6,435
Acute infectious encephalitis (082)	17	10	10	(1)	(1)	(1)	(1)	398	289	248
Influenza (480-483)	526	401	584	30th	275, 757	111, 383	181, 080	245, 227	75, 113	137, 522
Meningitis (085)	5, 164	4, 317	4, 317	35th	2, 295, 664	631, 323	569, 415	2, 276, 534	578, 930	533, 201
Meningococcal meningitis (057.0)	56	51	63	37th	3, 314	2, 941	3, 195	2, 401	2, 097	2, 223
Pneumonia (490-493)	888	808	(1)	(1)	(1)	(1)	(1)	57, 110	51, 759	—
Acute poliomyelitis (080)	665	1, 014	427	11th	3, 194	3, 968	2, 123	4, 328	4, 883	2, 590
Rocky Mountain spotted fever (104)	23	17	28	(1)	(1)	(1)	(1)	215	275	220
Scarlet fever (050)	333	309	604	32d	55, 502	79, 279	86, 862	39, 063	56, 735	60, 176
Smallpox (084)	—	—	—	1	35th	43	49	195	23	39
Tularemia (059)	16	17	28	(1)	(1)	(1)	(1)	546	676	568
Typhoid and paratyphoid fever (040, 041) <sup>1</sup>	88	106	106	11th	1, 086	1, 087	1, 187	1, 596	1, 575	1, 660
Whooping cough (056)	2, 363	1, 402	2, 176	39th	495, 638	40, 201	83, 683	474, 102	30, 168	53, 039

<sup>1</sup> Not computed.

<sup>2</sup> Indiana: Addition—measles, week ended May 27, 1 case; deduction—Rocky Mountain spotted fever, week ended May 27, 1 case.

<sup>3</sup> Including cases reported as salmonellosis.

<sup>4</sup> Tennessee: Addition—whooping cough, week ended July 8, 30 cases.

Central and the South Atlantic States. Texas reported the largest number of cases (124); New York, the second highest (44); and California, the third (39).

The total number of cases of influenza reported for the current week was 526, compared with 401 for the corresponding period last year. The cumulative total for the "disease" year (beginning with the thirty-first week, 1949) was 275,757 reported cases of influenza. The 5-year median was 181,080.

The number of cases of acute infectious encephalitis reported for the week was 17, an increase from the 15 cases reported for the preceding week. For the corresponding week last year 10 cases were reported. The cumulative total for the current calendar year was 398 which may be compared with the corresponding figure of 289 for 1949 and 248 for the 5-year median.

The total number of cases of Rocky Mountain spotted fever reported in the Nation for the current week was 23 compared with 24 cases last week and 17 cases for the corresponding week last year. The cumulative total for the calendar year to date was 215 compared with 275 cases reported for the corresponding period last year and 220 cases, the 5-year median.

The total number of cases of diphtheria reported for the current week was 60, the lowest total for the corresponding week in the past 5 years. The cumulative total for the current calendar year is 3,188 cases, the lowest number reported during the past 5 years. The 5-year low in reported cases of diphtheria is also shown by figures for the "disease" year which ended with the twenty-seventh week.

One case of anthrax was reported in Colorado. No cases of smallpox were reported in the United States.

### **Deaths During Week Ended July 15, 1950**

	<i>Week ended July 15, 1950</i>	<i>Correspond- ing week, 1949</i>
Data for 94 large cities of the United States:		
Total deaths.....	8,576	8,320
Median for 3 prior years.....	8,320	
Total deaths, first 28 weeks of year.....	266,026	264,454
Deaths under 1 year of age.....	629	617
Median for 3 prior years.....	640	
Deaths under 1 year of age, first 28 weeks of year.....	17,416	18,165
Data from industrial insurance companies:		
Policies in force.....	70,159,257	70,325,670
Number of death claims.....	11,972	12,698
Death claims per 1,000 policies in force, annual rate.....	8.9	9.4
Death claims per 1,000 policies, first 28 weeks of year, annual rate.....	9.6	9.4

**Reported Cases of Selected Communicable Diseases: United States, Week Ended July 15, 1950**

[Numbers under diseases are International List numbers, 1948 revision]

Area	Diphtheria (055)	Encephalitis, infectious (082)	Influenza (480-483)	Measles (085)	Meningitis, meningooccal (057.0)	Pneumonia (490-493)	Polio-myelitis (080)
<b>United States</b>	<b>60</b>	<b>17</b>	<b>526</b>	<b>5,164</b>	<b>56</b>	<b>888</b>	<b>665</b>
<b>New England</b>	<b>4</b>	<b>2</b>		<b>519</b>	<b>2</b>	<b>38</b>	<b>16</b>
Maine	1			3		17	2
New Hampshire				3			1
Vermont		1		1			
Massachusetts	3	1		363	2		3
Rhode Island				2		8	1
Connecticut				147		13	9
<b>Middle Atlantic</b>	<b>13</b>	<b>3</b>		<b>1,959</b>	<b>13</b>	<b>238</b>	<b>78</b>
New York	9	3	(1)	826	8	157	44
New Jersey				741	2	32	20
Pennsylvania	4			392	3	49	14
<b>East North Central</b>	<b>4</b>	<b>8</b>	<b>12</b>	<b>1,420</b>	<b>7</b>	<b>132</b>	<b>74</b>
Ohio		1	6	346		12	15
Indiana	2	1		49		5	5
Illinois	1	5	2	376	5	83	27
Michigan	1	1		178	1	29	19
Wisconsin				471	1	3	8
<b>West North Central</b>	<b>4</b>	<b>2</b>	<b>7</b>	<b>145</b>	<b>4</b>	<b>149</b>	<b>69</b>
Minnesota				61	1	8	8
Iowa				7	2		32
Missouri	2		4	33	1	6	12
North Dakota		1		23		127	
South Dakota		1		5			1
Nebraska			3			1	14
Kansas	2			16		7	2
<b>South Atlantic</b>	<b>7</b>		<b>117</b>	<b>143</b>	<b>5</b>	<b>26</b>	<b>118</b>
Delaware				8			
Maryland				5	1	21	3
District of Columbia				7	2	4	6
Virginia	1		84	58	1	32	32
West Virginia				11		1	8
North Carolina	4			11			20
South Carolina			21	4		4	28
Georgia	1		7	2		11	12
Florida	1			19	1	3	9
<b>East South Central</b>	<b>5</b>		<b>15</b>	<b>69</b>	<b>7</b>	<b>35</b>	<b>74</b>
Kentucky	2			18		1	23
Tennessee	1		11	10	2		26
Alabama	2		4	26	1	21	14
Mississippi				15	4	13	11
<b>West South Central</b>	<b>18</b>	<b>2</b>	<b>332</b>	<b>198</b>	<b>12</b>	<b>168</b>	<b>172</b>
Arkansas	1		30	19	4	4	10
Louisiana	1			3	1	10	12
Oklahoma	1	1	8	8	1	10	26
Texas	15	1	294	168	6	144	124
<b>Mountain</b>	<b>1</b>		<b>37</b>	<b>283</b>	<b>2</b>	<b>20</b>	<b>11</b>
Montana	1		2	4			1
Idaho			3	30	1		
Wyoming				8			
Colorado			6	135		6	4
New Mexico			2	8	1	3	1
Arizona			24	10		5	4
Utah				88		6	1
Nevada							
<b>Pacific</b>	<b>4</b>		<b>6</b>	<b>428</b>	<b>4</b>	<b>32</b>	<b>53</b>
Washington	1			40	1		10
Oregon			1	4		6	4
California	3		5	384	3	26	39
Alaska				2			
Hawaii				1			

<sup>1</sup> New York City only. <sup>2</sup> Anthrax: Colorado, 1 case.

**Reported Cases of Selected Communicable Diseases: United States, Week  
Ended July 15, 1950—Continued**

[Numbers under diseases are International List numbers, 1948 revision]

Area	Rocky Mountain spotted fever (104)	Scarlet fever (050)	Small-pox (084)	Tularemia (059)	Typhoid and para-typhoid fever <sup>1</sup> (040, 041)	Whooping cough (056)	Rabies in animals
<b>United States</b>	<b>23</b>	<b>333</b>			<b>16</b>	<b>88</b>	<b>2,363</b>
<b>New England</b>		<b>51</b>				<b>1</b>	<b>238</b>
Maine	2						51
New Hampshire	1						
Vermont	2						23
Massachusetts	39					1	74
Rhode Island	3						27
Connecticut	4						63
<b>Middle Atlantic</b>	<b>2</b>	<b>65</b>				<b>5</b>	<b>313</b>
New York	242					5	102
New Jersey	6						104
Pennsylvania	2	17					107
<b>East North Central</b>	<b>3</b>	<b>70</b>			<b>1</b>	<b>11</b>	<b>579</b>
Ohio	34					7	126
Indiana	5						28
Illinois	3	9			1	3	111
Michigan	15					1	159
Wisconsin	7						155
<b>West North Central</b>	<b>20</b>				<b>1</b>	<b>2</b>	<b>95</b>
Minnesota	3						19
Iowa	2						12
Missouri	7				1	1	35
North Dakota	8						
South Dakota							
Nebraska							
Kansas						1	26
<b>South Atlantic</b>	<b>12</b>	<b>26</b>			<b>2</b>	<b>13</b>	<b>302</b>
Delaware							3
Maryland	2	3			1	2	33
District of Columbia						1	9
Virginia	2	4				2	
West Virginia	1	1				1	102
North Carolina	4	16					39
South Carolina	2					1	68
Georgia	1	1			1	3	17
Florida						2	19
						1	10
<b>East South Central</b>	<b>1</b>	<b>22</b>			<b>1</b>	<b>11</b>	<b>83</b>
Kentucky	1	3				5	25
Tennessee		9				3	6
Alabama		7				3	43
Mississippi		3			1		26
						8	7
<b>West South Central</b>	<b>2</b>	<b>17</b>			<b>7</b>	<b>31</b>	<b>427</b>
Arkansas	2	1			6	2	30
Louisiana		2				2	
Oklahoma		2				7	33
Texas		12			1	20	362
							20
<b>Mountain</b>	<b>3</b>	<b>13</b>			<b>4</b>	<b>5</b>	<b>139</b>
Montana	2						8
Idaho		2					21
Wyoming							8
Colorado	1	3			1	1	26
New Mexico						3	20
Arizona		8				1	31
Utah					3		9
Nevada							16
<b>Pacific</b>		<b>49</b>				<b>9</b>	<b>182</b>
Washington		2					46
Oregon							49
California		47				9	92
Alaska							3
Hawaii							

<sup>1</sup> Including cases reported as salmonellosis.

<sup>2</sup> Including cases reported as streptococcal sore throat.

## FOREIGN REPORTS

### ANGLO-EGYPTIAN SUDAN

*Meningitis, meningococcal.* The approximate number of cases of meningococcal meningitis during the outbreak which occurred in Anglo-Egyptian Sudan January–May 1950, was 5,245. The highest incidence was reported in Darfur Province, where 3,840 cases were recorded. Khartoum Province reported 554 cases, and Kordofan Province, 310.

### EGYPT

*Meningitis, meningococcal.* During the epidemic of meningococcal meningitis which began in Egypt the latter part of 1949, the peak incidence (214 cases) was reported for the week ended March 18, 1950. The total number of cases reported January 1–May 27 was 1,745. This was stated to be the first time meningococcal meningitis has been reported in epidemic proportions in Egypt since the years 1931–34. The reported incidence for those years was 871, 4,508, 1,603, and 626 cases, respectively.

### CUBA

*Reported Cases of Certain Diseases—4 Weeks Ended May 27, 1950*

Disease	Pinar del Rio	Habana		Matanzas	Santa Clara	Cama-guey	Oriente	Total
		Habana City	Total					
Cancer	5		20	8	22	4	18	77
Chickenpox	1	20	29	2	4	15	11	62
Diphtheria		9	15	3				18
Leprosy	1		4		1			6
Malaria		1	1			1	19	21
Measles		4	5			7	12	24
Poliomyelitis					1			1
Tuberculosis	1		8	8	18	15	14	64
Typhoid fever	3	4	7	5	1	7	18	41
Whooping cough			5			1		6

### FINLAND

*Reported Cases of Certain Diseases—May 1950*

Disease	Cases	Disease	Cases
Diphtheria	46	Scarlet fever	849
Dysentery	61	Typhoid fever	15
Meningitis, meningococcal	9	Venereal diseases:	
Paratyphoid fever	72	Gonorrhea	524
Poliomyelitis	17	Syphilis	32

## MADAGASCAR

*Reported Cases of Certain Diseases and Deaths—May 1950*

Disease	Aliens		Natives	
	Cases	Deaths	Cases	Deaths
Beriberi.....			2	
Bilharziasis.....			32	
Diphtheria.....			2	1
Dysentery, amebic.....	12		104	1
Erysipelas.....			6	
Influenza.....	141		3,181	34
Leprosy.....	2	1	24	
Malaria.....	234	2	33,841	136
Measles.....	2		31	
Meningitis, meningococcal.....			7	
Mumps.....	1		99	
Plague.....			3	3
Pneumonia (all forms).....	4	2	615	123
Poliomylitis.....			1	
Puerperal infection.....			3	
Scarlet fever.....			1	
Trachoma.....			3	
Tuberculosis, respiratory.....	6	3	75	17
Typhoid fever.....	2		9	2
Whooping cough.....	2		269	2

### **REPORTS OF CHOLERA, PLAGUE, SMALLPOX, TYPHUS FEVER, AND YELLOW FEVER RECEIVED DURING THE CURRENT WEEK**

The following reports include only items of unusual incidence or of special interest and the occurrence of these diseases, except yellow fever, in localities which had not recently reported cases. All reports of yellow fever are published currently. A table showing the accumulated figures for these diseases for the year to date is published in the PUBLIC HEALTH REPORTS for the last Friday in each month.

#### **Cholera**

*Burma.* Cholera has been reported in Burma as follows: Week ended June 24, 1950, 36 cases, 18 deaths; week ended July 1, 45 cases, 27 deaths.

*India.* During the week ended July 1, 1950, 193 cases of cholera, with 69 deaths, were reported in Calcutta, and 15 cases (no deaths) in Delhi. One fatal case was reported in Lucknow during the week ended June 24.

*Pakistan.* For the week ended July 1, 1950, 14 cases of cholera, with 8 deaths, were reported in Chittagong.

#### **Plague**

*Belgian Congo.* On July 4, 1950, one fatal case of plague was reported at Indjoukwa (a village north of Blukwa), Stanleyville Province.

*China.* On July 7, 1950, 10 fatal cases of plague were reported in Amoy, Fukien Province.

#### **Smallpox**

*Belgian Congo.* During the week ended July 1, 1950, 134 cases of smallpox were reported in Belgian Congo.

*British East Africa.* During the week ended May 20, 1950, 98 cases of smallpox, with 21 deaths, were reported in Tanganyika Territory.

*India.* For the week ended June 24, 1950, 88 cases of smallpox, with 85 deaths, were reported in Calcutta, and 55 cases, 10 deaths, in Madrid; for the week ended July 1, 76 cases, 70 deaths were reported in Calcutta, and 54 cases, 11 deaths in Madrid.

*India (Portuguese).* During the week ended June 17, 1950, 16 cases of smallpox were reported in Portuguese India.

*Indonesia.* During the week ended June 10, 1950, 6 cases of smallpox were reported in Bandjermasin, Borneo, and for the week ended June 17, 11 cases were reported. For the week ended June 24, 194 cases, with 58 deaths, were reported in Surabaya, Java.

*Rhodesia (Southern).* During the month of May 1950, 55 cases of smallpox (10 deaths) were reported in Southern Rhodesia.

#### **Typhus Fever**

*Belgian Congo.* During the three weeks ended June 24, 1950, 24 cases of typhus fever (murine type) were reported in Belgian Congo, 11 of which were reported for the week ended June 10.

#### **Yellow Fever**

*Cameroon (French).* On July 6, 1950, one fatal suspected case of yellow fever was reported in Foumban Region, French Cameroon.

*Colombia.* During the month of January 1950, two deaths from yellow fever were reported in Colombia as follows: One death at Rio de Oro, Los Angeles, Magdalena Department, and one death at Putumayo Commissary, Mocoa.

*Sierra Leone.* During the period June 24-25, 1950, one fatal suspected case of yellow fever was reported in Koinadugu District.

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#### **Plague Infection on the Island of Hawaii**

Under date of July 12, 1950, plague infection was reported proved on June 26, 1950, in a mass inoculation of 10 fleas, collected from rats trapped in District 9A, Paauhau, Hamakua District, Island of Hawaii.

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## **Study of Laboratory Infection**

The first comprehensive survey to be made in this country of the incidence of infection among laboratory and research workers is now being conducted with the assistance of a \$3,200 grant from the Division of Research Grants and Fellowships of the National Institutes of Health, Public Health Service.

Dr. S. E. Sulkin and Dr. R. M. Pike of Southwestern Medical College, University of Texas, who are conducting the survey, will send questionnaires to all governmental and private laboratories handling infectious agents. Some 3,000 questionnaires, requesting information on numbers and types of infections which have occurred in individual laboratories in the past 20 years, have already been sent out; another 12,000 will be sent in the next few months.

The demands of modern medicine require increased numbers of laboratory technicians to handle potent disease-producing agents, both in diagnostic work and in research. As a result significant increases in laboratory infections have occurred, according to reports received by the Public Health Service.

The purpose of the survey is to determine how serious the problem is. No one knows how many laboratory infections occur among scientists who are dealing with diseases such as tuberculosis, tularemia, epidemic typhus, encephalitis, and Q fever. A channel for reporting such infections has never been set up.

The National Advisory Health Council, at its June 1950 meeting, unanimously recommended that such a survey be made, after studying a request from a private laboratory for funds to set up safeguards for workers on a Public Health Service-financed project. The Council felt that information on useful protective measures should be made available to all laboratories through a group study of the problem.

Dr. Sulkin and Dr. Pike will present results of their survey to the American Public Health Association at its annual meeting in St. Louis, October 30 to November 3. APHA has arranged a special symposium on protective measures against laboratory-acquired infections and, in addition to the report of the survey, will hear discussions of laboratory infections in tuberculosis, brucellosis and tularemia, mycotic disease, viral and rickettsial diseases, and of general laboratory safeguards.

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It contains (1) current information regarding the incidence and geographic distribution of communicable diseases in the United States, insofar as data are obtainable, and of cholera, plague, smallpox, typhus fever, yellow fever, and other important communicable diseases throughout the world; (2) articles relating to the cause, prevention, and control of disease; (3) other pertinent information regarding sanitation and the conservation of the public health.

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